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NATIONAL INSTITUTE OF
ENVIRONMENTAL HEALTH SCIENCES

NATIONAL CENTER FOR TOXICOGENOMICS

WORKING GROUP

NTP Public Meeting Report On
Carcinogens (RoC) Review Process

January 27, 2004

National Library of Medicine
Lister Hill Center Auditorium Building
Bethesda, Maryland

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NATIONAL TOXICOLOGY PROGRAM
REPORT ON CARCINOGENS PUBLIC MEETING
January 27, 2004

DR. PORTIER: Good morning, and welcome to the National Institutes of Health. I am Chris Portier, I am the Associate Director of the National Toxicology Program and I want to welcome you here today for the NTP public meeting on the Report on Carcinogens, peer review process here at Lister Hill Center Auditorium. It's my great pleasure to have you here today to discuss the process we are going to be use..., using for the 12th Report on Carcinogens, we are currently finishing up the 11th and we're looking forward to beginning our work on the 12th. It's always good when you have a important document that you're putting forth and a lot of public interest and stakeholder concern about how the process of that, that document is prepared. It's always good at the beginning to look at your process, think about it and carefully assess whether it still meets the needs for which the document was originally

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put forward and whether the process actually addresses exactly what you'd like to see it addressed. So today we're going to be discussing some of the very modest technical changes we've made in the preparation of background documents for the Report on Carcinogens and the review process itself. Dr. Jameson is going to do a presentation for that in a little while. Prior to Dr. Jameson's presentation Dr. Goldstein will remind us of a previous review we had on the Report on Carcinogens process and some of the recommendations that were made at that previous review and his opinion about whether we've addressed some of those recommendations or not, and I look forward to that presentation. I have a couple of housekeeping comments for you this morning that I'm required to tell you by the National..., by the Hill Center. No food or beverages are allowed in the auditorium, so those of you who have coffee with you quickly run out before the beverage police show up. No smoking is allowed anywhere in the building. That's true of the entire NIH

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Campus and all of the buildings in the NIH Campus. There are conference microphones at each seat, if you'd like to speak and you're recognized by the chair then I hope that you will press your button properly and a little red light should show up at the top of the microphone, Lynn, if you could press yours, everybody can see what it looks like..., there you go. When you're done speaking, press the button again and it will go off. If you don't press it we will hear all your rude comments in the background. If you have any presentation material, if you..., you, you're planning on putting something up, I would appreciate to make sure that you've touched base with Dr. Wolfe, Dr. Wolfe, if you'd stand right here, and she has copies of that so that we can think about them and look at them at a later date after your presentation and if possible get them handed out to everyone who is present. Finally, there are public phones in this building near the lobby, there are restrooms near the lobby, all of that is right where you came in.

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This morning in, to help guide us through this review and to interact with any of the public commentors, we've assembled a panel made up of some of our federal partners, some members past and present of the NTP's Board of Scientific Counselors. They're here to enter into the dialogue with you, to discuss some of the issues you're, you're bringing forth and to provide us with the Report at the end of the meeting as to what they saw and what they might think we should do with some of the information that was presented to us. Chairing the meeting for us this morning is Dr. Lynn Goldman, Lynn used to be a member of the NTP Board of Scientific Counselors, she has done a number of interesting jobs over the year, over the years, most notably Assistant Administrator of EPA for Pesticides and Toxic substances, was that it, assistant administrator?

DR. GOLDMAN: The official title is Assistant Administrator for Toxic Substances.

DR. PORTIER: Assistant

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Administrator for Toxic Substances. Now Lynn is at the Johns Hopkins Bloomburg School of Public Health in Baltimore, Maryland and she'll be chairing and we're quite happy to have her chairing the meeting this morning. She's done a number of interesting pieces of, interesting articles on the evaluation of evidence for a variety of toxic endpoints, looking at strength of that evidence and how you use that to make decisions about public health risks, and I think we're quite pleased and privileged to have her here with us today. Aiding Lynn in the, on the panel today will be, I'm going to go back and go through my list in order, Hillary Carpenter, from the Minnesota Department of Health. Hillary is a current member of the NTP Board of Scientific Counselors and again he..., we're very happy to have Hillary here today as well. He brings to us a very pragmatic State Public Health Official point of view in looking at this type of information and trying to make public health decisions on it. Elizabeth Delzell is here from the Department of Epidemiology, the School of

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Public Health at the University of Alabama in Birmingham. Elizabeth is also a member of the NTP Board of Scientific Counselors. She sits on the Report on Carcinogens subcommittee as does Dr. Carpenter, both of them are here to address some of your concerns and give us some advice, and again we're very happy to have Dr. Delzell here, here as well. Finally, we have Dr. Rafael Moure-Eraso, who is a former member of the NTP Board of Scientific Counselors, he sat on the Report on Carcinogens subcommittee as well. He's currently the professor and chairman of the Department of Work Environment at the University of Massachusetts in Lowell, Massachusetts. Rafael in recent months has been one of the few board members who has criticized us in public about the Report on Carcinogens process, looking at some of our criteria and some of the questions he has about how to use that criteria and we look forward to his discussion and comment as well. Sitting next to Dr. Moure-Eraso, I'm going to go back to my list so I get it correct here

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from the CDC NIOSH in Cincinnati, Ohio. Mark is the official NTP li... liaison from the NI...from NIOSH, the National Institute of Occupational Safety and Health. He's followed the NTP through a number of years, I believe he sits on the RG2 subcommittee which is the subcommittee of the NTP's executive committee that is part of the ROC process. Joining Mark eventually will be Bill Allaben from the FDA's National Center for Toxicological Research in Jefferson, Arkansas. Bill also has been, is the official NTP representative from the Food and Drug Administration and I believe he also sits on RG2 and has looked at the, the Report on Carcinogens process and voted on it through the years.

I'd like to thank a number of people for putting forth the effort to make this public meeting possible and through years of effort making the Report on Carcinogens possible. Bill Jameson and his staff at the NTP have very expertly handled, not only this meeting, but the entire Report on Carcinogens process for a number of years. Bill, where are you? There he is. And if you

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have any questions or comments afterwards, Bill will be available for discussion and listening to some of your points. Mary Wolfe and her staff in the NTP Office of Scientific... of... NTP liaison office and scientific review office also helped to put this public meeting together. If there are any reporters in the room who would like to have followup questions, I simply ask that you make sure that you touch base with Dr. Wolfe or a member of her staff before meeting with our staff so that we can keep track of who has met with whom and what discussions went on. Again, also if you have any documents or written comments that you'd like to give the program, please make sure Dr. Wolfe or a member of her staff gets them. Finally I'd like to thank one mem... one member of the audience who's come quite a distance, Dr. Ki-Hwa Yang from the Korean National Toxicology Program is here, they are trying to develop their own program in Korea and he's very interested in our public process of debate and discussion of NTP processes and documents. He's here not only

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for this meeting, but on Thursday, we are having another public meeting to look at the future direction of the National Toxicology Program and evaluate.... and begin the, a year wrong, year long process of developing a road map to achieve a different vision and a different direction, or an improved direction for the NTP. I'd like to invite all of you to that public meeting as well and I'm sure we have an announcement somewhere that we can give you of, on the logistics for that meeting. With that I want to thank you all for be here... being here and I'll turn it over now to Dr. Goldman who will chair this meeting from this point onward.

DR. GOLDMAN: Good morning, and welcome, I'm going to do something I've always wanted to do and call this meeting to order. It's really a pleasure to have the opportunity to chair this meeting today, I know that many of you have come here from long distances and braving our little snowstorm here, which probably from, for other locales doesn't look like much of a

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snowstorm, but, you know, snow like this can bring the Washington area absolutely to a halt and I hope that you had good travel and that, that you've been able to, to get around here. A couple of things, points that I want to make before going into our agenda, Dr. Portier already mentioned the importance of speaking into the mic, turning on your mic's. That's because this meeting is being recorded, both the presentations and, and the discussions and comments around it and, and so then also if you do enter into the discussion to give your name and so that, that would help the people who are transcribing or at least even listening to the, listening to the tape for preparing the minutes. Also that, since we are a small audience and this is a rather large room, those of you who are seated out in the, in the remote areas of this auditorium, you're more than welcome to move forward. You might have an easier time seeing the slides, hearing the presentations, hearing the discussion and um... honestly nobody up here is going to bite your head off or anything

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like that. This process is a very, very important process, it's a part of the Report on Carcinogens. I had an opportunity in participating in one back when I was a member of the Board of Scientific Counselors in the last go round of this and I can tell you that the comments that are made and the discussions here really make a difference in terms of improving the process for the Report on Carcinogens and, and in fact the Report of Carcinogens has very rapidly been evolving in its procedures over the last decade. I understand that most of that evolution has had to do with the very rapid change in the kind of scientific evidence that's available to the, to the reviewers, and that that has created changes that have allowed the incorporation and the consideration of, of newer scientific evidence. And at the same time I think that nobody involved in the process from, from what I can tell believes that, you know, that they have a perfect process that will never change, there's a real willingness to listen, there's real willingness to change

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and so I just.... I think that that's an important thing for everybody to understand in terms of a tone for the day. Also that there aren't very many of you here, we are hoping that unlike some of these meetings that we'll be able to have a little bit of exchange back and forth, that it won't just be a matter of, you know, one way street communications, listening, but that if there are things that members from the Board of Scientific Counselors or others of you wanted to elaborate on, draw out, have some further discussion on from the presentations that we're here and ready to do that. Since there are not very many people here, I'd like to start by very briefly going around the room, Dr. Portier introduced the people in the front of the room, but it's just, if you could quickly go around and give us your name, who you're with, that might be a nice way to start the day given that there are so few of us. So why don't we go ahead and get started and, actually we'll start in the very back and work our way forward, the folks who were finding their way through the

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building with me this morning...

COURT REPORTER: You spe... referring to us?

DR. GOLDMAN: That's you... you are...Yes, sir, are there any rows behind you?

COURT REPORTER: No, ma'am, there are not. My name is Todd Strader and this is Sean Burns and we are the court reporters who are preparing the transcript of your meeting today.

MR. SCOTT: I'm Dean Scott, I'm a reporter with BNA's daily environment report.

MS. SHOEMAN: Loretta Shoeman, OSHA, and I'll be moving up soon.

MR. SMITH: Darrell Smith, Vice President of Government Environmental Affairs for the Industrial Minerals Association.

MR. KELSE: John Kelse , Industrial hygienist, RT Vanderbilt Company.

DR. ROTH: Adam Roth representing Brush Wellman, a producer of beryllium and beryllium compounds.

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MS. LUDMER: I'm Jenny Ludmer, I'm here from Aspen Systems Corporation.

MS. BECK: Nancy Beck from the Office of Management and Budget.

DR. WOLFE: Mary Wolfe from the National Toxicology Program, National Institute of Environmental Health Sciences.

MR. NIDEL: Chris Nidel from Baron and Budd.

MR. YANG : My name is Ki-Hwa Yang from South Korea, I am working for the National Institute of Toxicological Research and I'm the head of the National Toxicological Program in Korea.

MR. KELLY: I'm Bill Kelly with the Center for Regulatory Effectiveness.

MS. LE HURAY: Thank you, I'm Ann Le Huray from the American Chemistry Council and I'm sad to report that Rick Becker is stuck in his neighborhood and won't be able to be here and he was going to present the ACC's comments and I don't have his slides, so we can figure out what to do there.

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DR. PICCIRILLO : Vince Piccirillo representing the Naphthalene Panel of the American Chemistry Council.

MR. BABBAGE : Michael Babbage from the Consumer Products Safety Commission.

DR. GOLDSTEIN: Bernie Goldstein, Graduate School of Public Health, University of Pittsburgh.

DR. PORTIER: Chris Portier, NIEHS/NTP

MS. THAYER: Kris Thayer NTP/NIEHS.

MS. FELTER: Susan Felter, Procter & Gamble.

MS. FISHER: Joan Fisher, Procter & Gamble.

DR. JAMESON: Bill Jameson, NIEHS/NTP.

DR. BUCHER: John Bucher, NIEHS/NTP.

DR. GOLDMAN: And there's one last person, if you push the button on your mic and we're just introducing ourselves.

MS. HURT: Valerie Hurt, Office of General Counsel.

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DR. GOLDMAN: Okay, well, without further ado then, let's get started and we're going to begin, as I said before, this is a... part of a continuum of these kinds of processes and we're fortunate that today Dr. Bernard Goldstein from Rutgers University is able to come... not Rutgers anymore, this is wrong on the agenda, University of Pittsburgh, School of Public Health is going to be able to review the last of these meetings and, and what transpired there.

DR. GOLDSTEIN: I don't want to say the last meeting was contentious, but I had to leave to go to a different university afterwards. The, I hope you all can hear me, and this is okay for the recorder. The, the last meeting was an example I think of openness and of a, just a fair exchange of views. Lynn Goldman started it off very well by saying two things: one is that the process... any process can be improved and certainly a process as complex as the one of reporting on carcinogens can be improved, and secondly

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that the NTP clearly felt that it had to respond to stakeholders, had to work with stakeholders in order to do its job and I think that's, that's a good way of setting a process up. A couple of things came out that were pretty clear, but sometimes were fuzzy, and I don't know if there's a better way of...turn some of the lights off, I'm not sure how well this can be seen .... anybody see a plug anywhere?

There's a control panel, is it there?

SPEAKER: Oh, God, now we're completely in the dark.

DR. GOLDSTEIN: But there, there were three sort of central issues which I think everybody agreed to, but they, they weren't always very clear in, in what people were saying. First, it's, it's very clear that, that some but not all chemicals cause cancer. If all chemicals caused cancer there wouldn't be a need to single out those, but that's, that's really sort of inherent in this. The second point is a point that has to do with the weight of evidence and that weight of evidence issue

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is one that I think has to be considered to be a setting for all the activities of the National Toxicology Program. I purposely picked the IARC one to make it clear that we're not talking just about NTP, we're talking about anything that uses weight of evidence where you have a continuum of the evidence and there is a continuum. We start at the bottom with compounds which we're reasonably certain do not cause cancer, your stuff goes to the top with compounds which we know and all agree upon cause cancer and then the amount of the evidence for every one of the others falls somewhere in a continuum, and what, in essence the regulatory process has to do is draw a line through that continuum, NTP has to draw a line through the continuum. Whenever you draw that line there are going to be chemicals that are just above or just below. So whatever the default assumptions are, there are going to be chemicals for which the evidence is sufficiently controversial, and controversial's too strong a term, for which the evidence reasonable scientists will

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differ slightly as to how they interpret the evidence, and inevitably there are going to be compounds like that. We are never going to be able to put all the compounds in boxes because we're dealing with the continuum and these lines are, if you will, artificial. So keeping that line and keeping wherever we hid that, wherever we put that line, reasonably consistently is a very important part of what the National Toxicology Program does for us. Now we have to understand that reasonable scientists will differ and there will always be controversy and there will always be, particularly with compounds like carcinogens, sufficient economic interest, sufficient political interest, sufficient public interest that there will be people who will be in making the big point about the fact that you, if you only interpreted this a little differently, it would be, now be above the line instead of below the line. There will never be a situation that I can imagine in which every compound will have complete agreement by every member of any scientific peer group such as the Board of

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Scientific Counselors, and that's built into the system. The third point having to do that, that's central that sometimes I don't think is arguable but we sometimes lose sight of it, everybody seems to say, and that it's clear that we're talking primarily about, about science, obviously there's more than science in where you draw those lines, but once you've drawn the lines, the identification process is a scientific one.

Well, the key points that were made, and I just pulled a few of them out of the long series of presentations, is that really everybody's in favor of compiling and publishing a list of carcinogens, nobody came in and said you shouldn't do it. You just have to understand that, that by and large the comments were appropriately focused on process. Now, some were not, some basically came in and said if only we had interpreted this chemical this way it would have been different. But by and large people were focused on how do we change the process, which is really what NTP is asking about. What's their process like, not what's a

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specific chemical that should have been done differently. I imagine some people here talked about that, but again I think you make your point much better if you say that this is an example of where the process could be changed rather than you should have interpreted my chemical differently. So by and large that was adhered to, and there were no recommendations in this very long document and major presentations to basically say that NIEHS should run this or that the NTP organizational structure should be different. There were a number of people from environmental groups which made comments that basically said we object turning over this process to the National Academy of Sciences or EPA or FDA, but nowhere in the record that I saw or in any of the presentations was anyone who suggested that we ought to do so. So there was sort of a, perhaps a feeling among the environmental groups that maybe the suggestion was out there, but the suggestion was not really made at the time of the meeting. There were obviously a lot of arguments about default

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assumptions, what do you accept, what don't you accept, in essence where do you draw those lines, that had to do, in the case of NTP between known and/or reasonably anticipated. There was obviously a lot of concern about, from the industry about the public would overreact, there would be unnecessary costs. There were some industry representatives who basically said that unless there was a unanimous vote, nothing should be called a carcinogen, be called a known carcinogen or even a reasonably anticipated to be, because it had such a tremendous impact on cost. There were others who said that really this is a regulatory decision because it has impact on OSHA's right to, on, on OSHA's right to, OSHA's worker language... basically you automatically stick a compound into a different card, category so OSHA regulates, EPA has a right to know, you automatically put it into a different right to know category, so there are regulatory impacts and because of these regulatory impacts there ought to be a much more of a regulatory

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approach to the document. Any comments that come in should be responded to by the A, by the NTP in writing rather than just simply taking note of.... all back and forth approaches are to occur as if this was a regulatory document. Not everybody... in fact it was probably a minority of people who were in favor of that, but generally that was an approach taken by a number of the industry representatives. Again, not all, that this ought to be much more of a document that has the give and take that we associate with an EPA regulatory document, where the process is everything. Lynn Goldman made a very good point about the, the fact that, that in regulatory agencies sometimes process is more important than substance, but then when we look at carcinogens, we really want to focus on substance, not process, and Lynn, I think I'm quoting you correctly, I think, in, in that. The public interest groups wanted the burden of proof to be on disproving carcinogenesis. The idea was that, that, that the cancer causing chemical is something that is such a tremendous

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burden to the public that in fact there ought to be a burden of proof, the default assumptions ought to be changed and such that we lean over backwards to say, yes, something is a carcinogen until proven otherwise, and there have been a number of comments about the NTP process since then in the form of the, of the precautionary principle. Now there are a lot of process issues, and what's...

SPEAKER: I'm sorry, I stepped on the...

DR. GOLDSTEIN: ...the concerns about the process had to do with everything from there being not enough time for full presentations to the Board of Scientific Counselors to not enough compound specific knowledge, to lack of acknowledgment of submissions to lack of specific response to submissions, to better publicity and, and better organization. There's a whole series of different issues to which I would suggest that NTP has at least partially responded to just about all of them. There is an increased time for presentation to the Board

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of Scientific Counselors, the compound specific expertise that NTP has in a sense consulted with in developing the documents is now, is now sitting at the table, the submissions are at least being acknowledged and, but there is still not this specific response to the submissions, there is still not a , if you will a, we've seen this, we've read it, here's what we've done about it, here's where we think you're wrong, here's where we think you're right, that would transform this into a regulatory process, and that remains as it was before. My feeling is, you know, my bias is to say that that's appropriate. The better publicized and more accessible to the public, NTP has responded by having meeting, this meeting in Washington during an ice storm to make sure everybody gets to it, thank you very much, but there is clearly an approach to, to make this more publicized. And some of the publicity issues have to do with a better understanding of the process. There was a real feeling at the last meeting by a number of the attendees that the Board of

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Scientific Counselors voted on the document, while the members of the Board of Scientific Counsel were there said, no, we don't vote on a document, the document is just one piece of the information, we might disagree in fact with part of that document, we're voting on this, you know, on this reasonably anticipated is it, doesn't, which category does it fit in and so that document should not be considered to be a document in which we unanimously approve. We're not approving a document, we're voting for a category and that distinction is a very important distinction and needs to be better publicized among others because otherwise the feeling is that they've approved the document, they've approved everything in the document when in fact that's not the way the process works. So these are a number of the, of the issues and what I would consider to be key, key points but which perhaps the most important ones that don't really fit under the process so much but fit under communication are these. There's a real concern about public misunderstanding. One of the more moving

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presentations was by Susan Dickinson from the Why Me organization, which is an organization of women who are concerned about breast cancer who basically said that Tamoxifen, when declared carcinogen by NTP, or considered to be in, in that process, that women who would have benefitted from Tamoxifen stopped taking the Tamoxifen. There was a physician here to testify from the drug company folks who were making it, basically testified that his estimate was that 50,000 women who would have benefitted, of the 50,000, I think he said 30 to 50,000 stopped taking it, I don't know if those numbers are right, but clearly we are dealing with a situation in which there's at least a potential for, for public health benefit, and there's all these dose and dose rate issues. One of the speakers brought some sand, a man representing the solar industry, brought some beach sand, he said clearly you don't mean that, well, clearly people don't mean that. Those dose and dose rate issues are issues that perhaps don't get communicated very well, but still silica

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is a carcinogen under the wrong circumstances, if you will, so that that issue of communication's important. The chemical form. Again, silica is a part of that, nickel was brought up, there are other chemicals, chromium, which is an essential nutrient in one valence and a carcinogen in another, is another issue that needs to be talked about, and the issue of a known human carcinogen, if we're serious about mechanistic information allowing one to say that this is a known human carcinogen, even though the epidemiological data isn't quite clear cut, you've got a problem with the word known. I think we in science understand what we mean to say when we say it's a known human carcinogen and we're bringing it from reasonably anticipated to known because of this mechanistic data, but again, publici..., being able to clearly communicate that is, is difficult.

Now I've got some recommendations that I've been told appropriately I should make as a member of the public, so I'm going to hold off making some of the

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recommendations that I actually made in the previous document that I'm going to stand on, but let me just say that I generally have been very, very positively impressed by how NTP has responded in thinking through the issues that people brought to them and in making changes. Now, they have not made a change which I would view should we put them into the process of being a regulatory agency and I think that they're absolutely right about that. But that is an issue that I'm sure will continue to be brought up and will continue to be reviewed by NTP as to how much they need to be responsive on a blow by blow basis, much like a regulatory agency, that being the central part of, of where the, where I see a difference of opinion among the, the people who we saw the last time. So good luck on this presentation, and I hope it works out as well this time as it did last time.

DR. GOLDMAN: Dr. Goldstein, before you sit down, first I, I assume that you have an early flight today so if, if you have new material that you'd like to

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present, would you like to present that after Dr. Jameson gives his review, we'd appreciate that and then second, just take a moment here if people have any questions about that present... about what you just saw and heard. Okay, thank you. Or comments, sure.

DR. MOURE-ERASO: Thank you, Dr. Goldstein, for a very interesting presentation. I really appreciate your perspective and I have two comments that, that, that I would like to, to, to present. The first one is I would like to reinforce your, your view that I don't think there is a substitution to the NTP as the agency that should be conducting this process. I believe that any other approach, especially ad hoc approaches would, the National Academy of Sciences or, or, or, or similar agencies would be that, a ad hoc situation, what we have with the NTP is a long history and a long institutional memory of how to do this and how to.... under the different problems that we are facing and, and is the agency that I believe is the most adequate agency

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to, to conduct this process and I want to make it clear that it's something that we should cherish and maintain and, and I don't think that, that the, the comments and criticisms that sometimes people present in the process as mine, for example, are not meant to undermine or attack the mission of the agency that I consider that is irreplaceable and, and, and that has done an excellent job. The other comment that I have is that you, you mentioned your, your concerns out of the 99 last session like this on the fact that some... the, the public health value of some substances that because they are listed in some form as a carcinogen are going to remove that substances from circulation in society and those substances sometimes could have obviously very good public health effects. However, I think that, that, that we could never forget that the most important function is, is not how some substances listed have some, might have some good effects in one form or another that doesn't consist cancer, but that the principal function is the

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public health effect of listing the substance and the public health effect of protection that happened in society with a substance that's specifically identified and put it in the list. You started by saying that it's important to have list... I fully agree with you, it's important to have list, so, so that public health function I think is, is starting out really important, so thank you very much.

DR. GOLDMAN: Okay, all right, thank you, thank you, there's one more comment.

MS. FELTER: Susan Felter. It's a question. Are transcripts available on NTP's website or anywhere else from that 1999 meeting?

DR. GOLDMAN: The question is whether there's a full transcript available from the 1999 meeting. I think that what's, what we have are the, we have minutes that were posted, but Bill?

DR. JAMESON: Yes, the, the transcript from the, from the 1999 meeting actually are on, on our website. If you go

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to our website and go to the part where we discuss the 1999 meeting, the, the transcript is there.

DR. GOLDMAN: Excellent, okay, Bill, why don't you come forward now and Bill is going to give us an overview of the history and review process for the Report on Carcinogens.

DR. JAMESON: Well, thank you and good morning, I would like to also welcome everybody here and, and thank you for braving the elements to come in and participate in this meeting. I'd like to thank Dr. Goldstein for his presentation, I think he, he presented a very clear and concise summation of what was discussed at the meeting and what I plan to do here is to go through the, the proposed process and identify where we have made some changes or revised our process in response to the 1999 meeting. Kind of repeating some of the things that Dr. Goldstein has talked about in his presentation.

First of all, just as a kind of an introduction, the Report on Carcinogens is

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repaired, prepared in response to the Public Health Service Act that was passed in 1978 and that Act stipulates that the Secretary of Health and Human Services shall publish an annual report that lists all substances which are either known to be human carcinogens or reasonably anticipated to be human carcinogens and to which a significant number of persons residing in the United States are exposed. This law was amended in 1993 to, to make it a biannual report. Mainly because of the time involved in putting it together, we, we had a very difficult time getting the report together on a, in a one year period. What I put up here and actually this is some material that was, that's provided to you in your packets or, or out front is, is the criteria and I, I specifically made a slide of the criteria as it's published on the web page so that everybody can see what the, what the basis is of listing materials either as known or reasonably anticipated human carcinogens. Very briefly, I don't want to read all of the criteria, but very briefly, okay, for a

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known human carcinogen there must be sufficient evidence from studies in humans which indicate a causal relationship between exposure and, and human cancer. For the reasonably anticipated category, it can be limited evidence in, in, from studies in humans. But there are other situations where confounding could not be completely eliminated from, from the evidence or there is sufficient evidence from studies in animals... in laboratory animals where an increased incidence of malignant or a combination of malignant and benign tumors are, are induced by exposure to the particular material, or there is less than sufficient evidence of carcinogenicity in humans or laboratory animals, but the nomination or the material belongs to a well defined structurally related class of substances whose members are listed in previous Reports on Carcinogens as either known or reasonably anticipated carcinogens. And the paragraph in the box, if you will, that conclusions regarding carcinogenicity in humans and experimental animals are based on

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scientific judgment with consideration given to all relevant information, and this is an important point because when the criteria was revised in 1996 the inclusion of consideration of all relevant information meant that, that mechanistic information was a, was an integral part of the review for listing something in the Report on Carcinogens. At the time that we were putting together the 9th, excuse me, Report on Carcinogens there was a number of comments that were coming in that people were confused by what exactly did we mean by human studies. And so we published a clarification in the Federal Register, which is, which is shown, shown here and basically what it, what it indicated was that some question had arisen about what we meant by human studies to be listed as a, as a known human carcinogen, and that the known human carcinogen requires, I want to read this to make sure I don't make a mistake, the known human carcinogen category requires evidence from studies in humans, this can include traditional cancer epidemiology studies, data

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from clin..., clin..., excuse me, clinical studies and/or data derived from the study of tissues from humans exposed to the substance in question and useful for the evaluating whether relevant cancer mechanism....mechanisms is operating in people. So we just wanted to clarify what was meant by human studies.

In this slide I, I put up the review processes, we discussed it at the 1999 meeting and I wanted to use this as a basis to say most of the comments and issues that were brought up dealt with the nomination and the preparation of the background document which is essentially this part of the process before it goes on to the scientific review by the three review committees, which include the NIEHS review committee or what we refer to as the RG1, the interagency working group, which is made of representatives from the NTP executive committee or the RG2 and the NTP Board of Scientific Counselors ROC subcommittee which we refer to as our external peer review meeting, which is, which is held in a public

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forum. So what I'd like to do is to really address what changes or modifications we've made to the process since 1999 in the following slide.

First, I want to discuss the nominations. As, as in the past we always solicit nominations from the outside, we go out with announcements in, on our NTP list server, we take advantage of Federal Register notices when we're anouncing new nominations to ask people if they have other nominations that they want us to consider to please submit them to the NTP for consideration for listing or de-listing from the Report on Carcinogens. At the time of the 1999 meeting, the evaluations of the nominations for formal review, at the time I took advantage of, of the RG1, the NIEHS review committee to help me identify the nominations and make sure that, that there was sufficient preliminary information for a nomination before we proceeded with getting approval to review a nomination for listing in the report. Well, one of the modifications are... that we are making for

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all future Report on Carcinogens, and Chris Portier was, was, pushed that we, we make this a separate operation. We've established an NIEHS nomination committee, which is independent of the RG1. This NIEHS nomination committee is made up of NIEHS staff scientists who get together and review the list of nominations that my staff have been able to pull together from solicited nominations from outside or from nominations that, that we've been able to identify by our perusal of the, of the literature or the publication of other documents such as IARC or EPA identification of, of potential carcinogens for listing in the Report on Carcinogens. This NIEHS review committee looks at all the preliminary information we are able to gather or have been, or was submitted with the nomination and they say in their opinion there is sufficient information for us to pursue a formal review of the nomination. Once we, we go through that exercise, first we go to, to Dr. Portier as Director of the Environmental Tox program and, and get his approval and then

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we go on to the director of NTP who ultimately has to give us his okay that we can proceed with a formal review of the nominations. Once we get the okay, the approval from the Director, we go out with a Federal Register announcement with our intent to review a particular nomination and we solicit public, public comments on the nomination and we specifically ask at this time for, for any people who have an interest in, in the particular material we're looking at to identify issues that we need to address in the course of our review of the nomination. This was one of the issues as Dr. Goldstein indicated that at the 1999 meeting that, that people indicated that, that issues surrounding the nomination needed to be identified. And we go out with our Federal Register notice announcing that we intend to review these materials for possible listing or de-listing from the Report, and we solicit anyone with any information to please identify the issues that they feel are important for us to consider in the, in the course of our review.

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As with all public comments that, that we receive concerning the solicitation of information, the comments we receive on a, on or for a nomination are placed on the web and become part of the public record. In addition as par... as part of the review process all the review committees also get the, any public comments that we've received in the course of their review, included in the package are the public comments we received in response to comment for a particular nomination. Another area where we have made a number of changes for the, for the process is in the preparation and distribution of the background documents that we prepare for each of the nominations. Briefly when we say that the background documents are prepared with the, with the support of a, of a contractor that we have for the RoC process or for the RoC group and taking the recommendations that were identified or acting on some of the recommendations that were, were, were made at the last meeting, the 1999 meeting, excuse me... I'm sorry.... based on some of the,

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some of the comments that were made in the 1999 meeting we have increased our effort to try to identify outside experts that would be willing to help us in the preparation of these background documents. And, and to, to try to elaborate on this, I've broken it down as how, how we have revised the process that we've gone through the, the nominations for the different editions of the Report on Carcinogens. For the 10th Report on Carcinogens, some of the background documents were drafted or reviewed by, by nomination specific experts. As we initiated our work on the... on the 10th back in 1990...1999, I'm sorry, 1998 and 1999, we made a concerted effort to try to identify experts that, that had some experience in, with a particular nomination and solicit their help in either preparing different sections of the background document or at least reviewing a background document and giving us their comments as to the adequacy of the, of the information contained in the background document and the issues identified in the document. The way we identify these experts

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is basically is to do as thorough a literature search as we can on the substance and identify people who have published extensively on the material in the literature and go to these individuals and ask them if they'd be willing to help us.

So the background document is prepared and for the 10th Report on Carcinogens and again in, this is in response to some of the comments that were made in the 1999 meeting. The background documents are revised, were revised after the RG1 and then also revised after the RG2 meeting so that, basically the comment was that, that by doing this, providing the public comments to the RG1 they could look at the public comments, look at the background documents and comment on the document and, and make recommendations for revisions if necessary and the same for RG2. So in response to that comment that's why we did this particular process for the 10th Report.

After the RG2 had completed their review of, of the nomination and made their

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recommendation, then the background document became the document of record and was put, made available to the public. Either we may, we put out a Federal Register announcement indicating that the documents were available and if anybody wanted to get a copy to, we'd be happy to send one to them, and then we also put them up on the web site, excuse me... and made them available to the public and this was at least 60 days before the Board of Scientific Counselors, the RoC subcommittee met to review the nominations giving, giving people time to, to look at the background document before the public meeting and giving them the opportunity to come to the public meeting knowledgeable of what was in the background document and being able to make their comments at that time.

For the 11th Report on Carcinogens...oh, by the way, the 10th Report, the 10th edition of the Report on Carcinogens was published in, in 2002. For the 11th report, we, we, before we started our reviews, we stepped back and, and looked

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at how things were working and actually it was at the insistence of Dr. Portier that he felt that we needed to make the background document available to the public earlier in the process than waiting until the RG2 had completed it. So, for the 11th Report on Carcinogens most of the background documents were drafted and/or reviewed by nomination specific experts. I think we, we prepared 13 background documents for the nominations under consideration for the 11th and, and all but two had input from outside expert consultants, two we, we just could not identify anybody to help, help with those two background documents. For the 11th report, once the RG1 had reviewed the background document and, and said that the background document was acceptable for reviewing the nomination, applying the criteria and making a recommendation, then we identified that or I identified that as a document of record and it is at that point that we try to make it avail..., we tried to make it available to the public as soon after that as possible. By doing that, we

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have more consistency... we allow the, the reviewers of a nomination to have the same document to review and to make their recommendations, so all three reco..., all three scientific review groups have the same document of record to look at and to apply the criteria and make their recommendation. For the 11th Report on Carcinogens the background documents or records were made available on the NTP website either right after the RG1 review, 9 of the 13 background documents were up on the web right after RG1 review or 4 of the 13 were up on the web after the RG2 review, after the second review, but all of the background documents for the 11th Report on Carcinogens were up on the web and people notified of their availability at least 90 days before the, the public meeting of the RoC subcommittee.

For future RoC nominations, what we plan to do is to continue to prepare the background documents with the assistance of nomination specific experts. We again will try to identify individuals who'll help us prepare or at least review the background

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good thorough document. The RG1 again will, will be asked to look at the background document and to give us their opinion as to the adequacy of the document for reviewing a nomination, applying the criteria and making a nomination... or making a recommendation, excuse me. Once the RG1 has, has looked at the background document and, and said yes, we will accept this document for our review of the nomination, what we will now do is we will take the background document and publish it on the NTP website and it will be on the NTP website for at least 45 days before any review of a nomination takes place. So before the RG1 review takes place, the background document will be available on the web, are made available for people to see and, and if they care to make, make any comments, we'd, we'd be more than happy to receive them.

Moving on to the actual review process, the review process itself is other than, than the availability of the background document and, and the RG1's involvement in looking at the background document and making

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an acc... I'm sorry, accepting the background document for the review of the nomination, the review processes continue, will continue to remain pretty much the same. The first review is by the NIEHS review committee, the RG1, they will review the background document and make their independent recommendation for, for listing or, or not listing or de-listing depending on what the nomination was for. After the RG1 review it'll go on to the RG2, the Executive Committee interagency working group, they will be given the same document of record and they will review the nomination, apply the criteria and make their recommendation. Following the, the RG2 review as, as has been the process in the past, we will send out a Federal Register Notice announcing the public meeting of the Board of Scientific Counselors RoC subcommittee. In that announcement we will, we will invite individuals to come attend the meeting and if you care to make a public comment, to please come to the meeting and, and address the, the nomination to the committee. In response to some of the

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comments that were made at the 1999 meeting and as Dr. Goldstein indicated, we have increased the time allotted for people to make their comment to the Board. Initially, initially it was people were limited to five minutes, we've expanded that to seven minutes and at the discretion of the chairman can be expanded to up to ten minutes depending on how many people we have commenting on a particular nomination. So we've expanded the, the amount of time that people can, can address the, the Board during a public meeting. Again the Board subcommittee listens to the public comments, any written public comments that we receive in response to this particular Federal Register Notice, that information is also provided to the Board of Scientific Counselors and, and published on the NTP website and is made part of the public record and the board reviews the nomination and makes their recommendation. Following that recommendation, we go out with our third and final Federal Register Notice concerning this particular set of nominations where we solicit final public comment on, on

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the nomination and we include in the Federal Register all the recommendations that have been made by the three scientific review groups. We include what the recommendation was and what the vote for, for the recommendation was. Following receipt of the, of the public comments from the final Federal Register Notice, we take all the recommendations to our NTP Executive Committee. Our NTP Executive Committee looks, reviews the nominations, discusses the, the recommendations that have been made by the three scientific review committees and then make their own recommendation to the Director for listing, not listing or de-listing depending on what the nomination was. Following that review, all of the information, all three review committees' recommendations, all the public comments that we've received, the recommendation of the NTP Executive Committee itself, all this information is pulled together and we bring it to the Director of the NIEHS/NTP for his consideration and his final recommendation as to what should be included in the report

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and, and in what category. After the Director of NIEHS/NTP makes, makes his final determination then the, the, the draft of the final edi.... of that edition of the Report on Carcinogens is, is completed and forwarded on to the Secretary's office and the Secretary's office takes the, the reports with the recommendations for, for the listings, reviews the document. The process is, a lot of times is the Secretary's office will come back to us with questions for clarification or whatever and then once the Secretary is, is satisfied with the document it's, becomes the final document and is forwarded on to, to Congress. And, and when the Secretary forwards the report on to Congress is our definition of when the report is published. Requirement is, like I said, every two years, the 11th report I forgot to mention that we just completed all our reviews. The 11th report is scheduled to be published this year in 2004 and we're currently going to start working on the 12th report, which would be due in 2006.

Just to follow up, in our response

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to the, to the 1999 meeting that was published on the web there were several issues that were identified as under consideration and I just wanted to very briefly go over these and, and bring you up to date on the status of them. The first one was to create separate groupings within the Report on Carcinogens according to intended use. This was a recommendation that had been made by, by a number of individuals and we addressed that, we, we actually, when we were preparing the 9th Report on Carcinogens, we, we addressed having the categories separated for intended use, but after looking at the report, getting input from, from our NTP Executive Committee, from the Board of Scientific Counselors and also from the Secretary's office, it was decided that the current format of the Report on Carcinogens where we just listed the material in the two categories is, is the most appropriate, and, and so we will continue to do that for, for all future reports for the time being. The other two were, were issues that, that Dr. Goldstein emphasized in his

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talk, one was to ask applicable regulatory agencies to consider communicating information about possible regulatory implications of listing and de-listing and the other one was to work with regulatory agencies to identify additional venues and strategies for targeting communications about policy with broad group of stakeholders. We continue to work with the regulatory agency representatives within the Executive Committee and on our review committees to, to pursue this. There have been some, some examples where when we listed materials, we have joint statements by both the NTP and the regulatory agency about a particular listing. For example, the Tamoxifen as, as Dr. Goldstein brought up. When, when Tamoxifen was listed in the 9th Report on Carcinogens, when the report was released, a statement, a joint statement was released by NTP and FDA and then NCI about Tamoxifen and, and while it has been shown to be a human carcinogen, it also has very beneficial uses for the treatment of ca.. of breast cancer and that individuals should in

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consul... in consultation with their physician do their own assessment as to the benefit of taking or not taking the material. So we do work with our regulatory agencies to try to address these two issues and we will continue to do so in the future, and that's it from me, and I'd be glad to try to respond to any questions.

DR. GOLDMAN: Yeah, Bill, I'm going to go ahead and lead off with a couple of questions. First I wanted to make more of a comment that I hope just makes it very clear to the people in the audience exactly where today's meeting fits in with various Reports on Carcinogens, because I think it's always important when people are coming in and, and, and in participating for them to know what they can actually affect and what they can't affect, and my understanding, and correct me if I'm wrong, is that the 11th Report on Carcinogens which is due to come out this year is basically in its final stages of having recommendations brought forward to the Secretary for the Secretary's decision, and that this meeting cannot affect

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that process, because that process is nearly completed. However, that the 12th Report on Carcinogens has not yet gone into the scientific review process and that in fact this meeting can affect the review process for the 12th report, is that correct?

DR. JAMESON: That's correct.

DR. GOLDMAN: So, just so that people understand, you know, that... I mean if you have a need or wish to have an effect on the process for the 11th Report, there probably are ways to do that and... but not this particular meeting, is not a way to do that, and could you be precise about where that 11th report is at this phase, has it gone through the Executive Committee, is it with the Director of the NIEHS?

DR. JAMESON: The... as it stands right now the, the, the... when we, when we, let me back up just for the point of clarification, when we review nominations for the, for a particular edition of the report, for the 11th report, we usually break the nominations into, review half of them or

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a portion of them one year and then the second half the second year. We've completed review of all the nominations for both the first half and the second half and the second half... we, we are taking those to the Executive Committee in February and, and then hopefully very shortly thereafter we'll have all the information we need and can present it to the, to the Director.

DR. GOLDMAN: Okay...

DR. JAMESON: At that time, right, shortly after that.

DR. GOLDMAN: ...so that's kinda where it is just so that people know that some of it has gone to the Executive Committee, some of it's going to go to the Executive Committee and is on its way to the NIEHS Director, and so in terms of the 12th report though, that it's going to be... this isn't, you know, very much, very timely...

DR. JAMESON: Right.

DR. GOLDMAN: ...and, and can, and can have an effect. The, the other thing that I wanted to, to raise really is just as a point of clarification...

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DR. JAMESON: Mm-hmm. (Indicating affirmatively.)

DR. GOLDMAN: You said that prior to beginning the scientific review process that the RG1 looks at the background document to see if it is suitable for the scientific review process, and if it is suitable then it will be placed on the web for 45 days before that process begins. What if it isn't suitable, what is the process that you use?

DR. JAMESON: Well, if, if we bring it to the, to the RG1 and they look at the document and they tell us it doesn't contain sufficient information for us to apply the criteria, it doesn't contain... We c.., we cannot apply the criteria because it's lacking in information in either the, the animal section or the human section or something, then we would have to go back, address their concerns, work on it again and, and revise it and bring it back.

DR. GOLDMAN: Okay. Dr. Portier?

DR. PORTIER: Yeah, Lynn, I

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want to give you a little bit about my philosophy on this and where we're leading the program on this, but also some additional clarification. First of all, the 45 days is a target, it's not an absolute. But Bill said at least 45 days, well, that's our target, I want to make that very clear. We're going to try to achieve a 45 day lead time, but since the RG1 meetings are not regularly announced, they're not public meetings anyway, we're, we're... it could be well in excess of that or it could be potentially slightly less, but that is our target for that. The second issue is the, the question of the acceptability of a document and what we're trying to do here with the process. If RG1 looks over a document and concludes it's inadequate for the review, that can happen two different ways, one is that the NIEHS nomination committee made a mistake and RG1 is in disagreement with them that there's enough information here to do a... to list a compound. That would not disqualify the background document and we may well continue

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hopefully if all the review committees were doing the same thing they'd all say insufficient evidence to list, don't put it on the list. If on the other hand they find factual problems with the document, factual errors of interpreta.... of, of presentation because hopefully our experts are not interpreting the material for us, they are presenting the material to us, then in fact that would go back for clarification and correction. One thing Bill also forgot to mention is that once the document becomes the document of record the NTP does not intend to change that document, but the document will build, as we receive public comments on the document, they will be appended and noted that they are appended to the document for any future review groups. The issue here is that I feel fairly strongly that it's not up to the program to interpret the public comments that are coming to us as part of these, this review process. We have three very competent review groups that provide us with advice on this issue, we leave it up to them to interpret the, the

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to the background document that we have here. So they get appended and they get noted and we do our best to try to bring them to the attention of our review groups as they begin this review process. Again the philosophy is, the program is not responding to these public comments, nor do we actually own the background document, it's, it's something to facilitate the discussion and facilitate the review and we want it to be as scientifically correct as possible.

DR. GOLDMAN: The, the last question that I wanted to, to put to you before opening it up for more questions and discussion is the role as you see it of the NTP Executive Committee in this, and I'm, I, I'm realizing from the written comments that there are comments about this, but I think that it might be important for you to explain what role, what function that step has and how that's different than the RG1 and 2 processes and Chris, maybe you would like to respond to that?

DR. PORTIER: Yes, I will.

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I, I guess I should have brought slides of what is the NTP to lead us into this. The National Toxicology Program is not one agency, it is not just NIEHS's own little project, it's a multi-agency federal program, three agencies form the core, they're all within HHS, the Directors of those three agenc..., agencies sit on the Executive Committee of the National Toxicology Program, that is NIEHS, FDA and CDC NIOSH, their heads or their designates sit on the Executive Committee. The Executive Committee is also making a recommendation to the Secretary through the Director of NIEHS about the listings in the Report on Carcinogens, so their opinion is very important to the final recommendations that go forth from the Director of NIEHS to the Secretary of Health and Human Services. Other members of the Executive Committee are not necessarily part of HHS, but again represent some very important federal partners as part of the NTP and contribute substantially to our process and our evaluations and all aspects of the program, and so their opinion is

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sought as well. The Executive Committee may or may not vote on a particular nomination as to whether or not the Director should choose one decision or another. All of the discussions that go on at the Executive Committee are privileged, they are federal agencies talking to federal agencies so I'm not going to get into a lot of detail about how that process works and what their actual role might be because it changes depending upon the agent we're looking at, and what our concerns may or may not be on that agent, does that help, Lynn?

DR. GOLDMAN: Yeah, and I can... I can make, you know, a brief comment, I chaired that committee for a while, and I'm not with the federal government and I never signed a statement saying I wouldn't talk about what happened there, and it, it was not a technical review process in the way that the RG processes were. It was on a different level, it, I think, was useful to Dr. Olden to hear from the leadership of the other agencies what they thought, because it's a lot of weight

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on his shoulders to make the recommendation to the Secretary, it helped to bring out into the open, if there were any possible disagreements or issues to have that out in the open as opposed to people, you know, individually going to the Secretary and expressing their views. It's a healthy process to have those different views aired around the table instead of handled that way. And it did help to surface things like the Tamoxifen kind of concern that, gee, if this is listed it might help to have a statement from the FDA about what it means and to try to head off inappropriate responses by the users of the product down the line that they would overreact possibly to the listing, so I, I, I, I felt that it played a useful role, but I think that it could probably be a little bit more clearly explained what that role is having seen, you know, some of the comments and that's why I wanted to kind of bring that out. Opening the mic's here for other questions or comments for Bill Jameson about the process and how it's changed and what might be

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contributed here today.
SPEAKER: Focusing just a couple of questions following up what Dr. Goldman asked. The, if, if the background document is accepted by RG1 as the, as the document of record, does that mean that the word draft shouldn't be on the cover? 'Cause sometimes they say draft and then they're not revised.
DR. JAMESON: Right, that, that's correct, there are, we have some, some... we need to clean up our website, there are some there that still have draft on it that, that should be final, thank you.
DR. GOLDMAN: And just a reminder to identify yourselves if you have questions or comments.
MS. LE HURAY: Okay. Well, I'm Ann Le Huray with the American Chemistry Council, and following on that, I guess that I don't understand two things about that process with the document of record, or three things actually. One is why would it be inconsistent with making of the document of record to have a round of public review

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final. I don't understand why that would be inconsistent with the process. Second is if there are in fact, you know, if you don't have a round of public review and it comes out with errors in it and then you say, you know...and subsequent you build on it by attaching public comments to it, how, how is that consistent with the Data Quality Act, you know, you're putting out information there that is incorrect, and even though you're putting in public comments that may have corrections, that, that's different than having a document with NTP's name on it that contains incorrect information, and thirdly by calling it the document of record that implies that reviewers after the RG1, for example, RG2 and the BSC subcommittee will be using that document as... to form the basis of their decisions, but what if.... perhaps RG2 wouldn't, because as Dr. Goldman says perhaps it's not as technical a review, but what if the.....
DR. GOLDMAN: I meant the executive com... not the RG2. The RG2 is technical. I'm sorry if I, if you heard me

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that way, it's the Executive Committee that's their higher level people and agencies.
MS. LE HURAY: But, but the Board of Scientific Counselors subcommittee, they, they bring their own thoughts about what is or isn't scientifically important about a nomination to the review and if they disagree or have issues with the way something is presented in the background document, that's never appended anywhere, that's never recorded anywhere, so that can... that just becomes an ephemeral and even if it's the basis of their decision that's just an ephemeral point, so...
DR. GOLDMAN: Well, I think, I think we can take most of that kind of as a comment, I think that, you know, those are points well taken. Dr. Jameson, are there points of clarification that you want to make?
DR. JAMESON: Just to, to address your last point about if... if review committee looks at a background document and fear..., and feels that the background document is not... doesn't contain

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to, something added to the, to the document, we have, we have allowed for that, in fact there, there have been background documents that we reviewed for the 11th report and I should have mentioned that in my presentation and I apologize. If, if a review committee, the RG1, the RG2 or the board gets a, a background document and reviews, reviews a background document and they feel it is inadequate because it didn't contain enough information in a particular area, if they felt that we...a particular paper was not included that should have been included, whatever...we give, we give the, each of the, each of the review committees the opportunity to, to write a commentary about the background document, and that commentary then becomes part, part of the record for, for the nomination. And in fact the RG2 did that for our review of Cobalt Sulfate. They felt that, that the information in the background document on, on production and use of Cobalt Sulfate was insufficient and unclear and they felt strong enough about that that they, they prepared an addendum or

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a commentary to, to the background document and that became part of the public record. So as the, as the document goes through the review committees, if the review committees have a serious concern about the, the, the, the background document, they feel something is left out or, or should have been included or added, then, then that can be appended to the document as a commentary from that particular review group.

DR. GOLDMAN: Were there any other... wait, I think there was one more comment from the audience and then, before we go to the... I'd like to take the comments from the, from the audience first.

MR. KELLY: Bill Kelly with the Center for Regulatory Effectiveness. It occurred to me on my way to the meeting just today that although we submitted detailed written comments on the process there was a significant issue that we had totally overlooked and that hasn't been spoken about today. And it may have to do with just the way that the procedures are written up that talks continually about a background

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document, previously addressed background document, but I know on a number of occasions the way the actual listing is written and put in the Report on Carcinogens does not... is not necessarily the same as what's in the background document. I know a number of chemicals for which the actual listing language has changed after the entire review process was finished and so the question is when does the public learn what the listing is actually going to say and should it not have an opportunity to comment on that actual listing language, or should the background document in effect say, this is what we're proposing as the actual listing language and then again that raises the issue of well, if this is the final document of record, what does that mean with regard to the listing language, does that mean it can't be changed after that or, or what? But there is this difference between background document and the listing language that goes in the final RoC and the public's opportunity to comment on that. Sometimes it can be very important, there are subtleties

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just in the way things are worded just in that first paragraph of the listings. One example that comes to mind is alcoholic beverages and I'm not sure whether that is one of the ones that got changed slightly from what was in the background document, but that's a good example. Exactly how that was phrased in terms of the quantity that might be known to induce cancer was an important issue and there were some subtleties in the wording of that particular listing in the RoC. So that, that issue of when do we see the language of the listing and when do we get a chance to comment on that has not specifically been addressed, perhaps you could comment on that.

DR. JAMESON: Well, maybe we could.... maybe that's something we, we need to address in the future, we'll see. I'd like to see what we get from the rest of the meeting and, and identify these issues.

DR. GOLDMAN: Chris?

DR. PORTIER: It, it does point... I, I think it's a suggestion worth considering and we will, we will give it

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our, our best consideration. I did want to point out one thing though. The, the historical background documents did in fact come into the review process with a flavor in them of where this review was going. So there was some suggestion as you read the documents that this probably should be reasonably anticipated or this probably should be a known human carcinogen. Part of this splitting I'm having between RG1 and the development of the, of the nominations in this independent background document production is in fact to cause that separation. So whereas historically there might have been some indication of the, in the background document as to what would go into the final RoC document, that is not required nor is it suggested nor should it actually scientifically be there. The background document should be facts, statements about the evidence that's, that's there, but no objective evaluation of whether it should be listed or not. And since the final listing in the RoC is a discussion of the final opinion of the Secretary as to

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whether it should be listed or not, it's, it's not necessarily something that would be reflected in the background documents anymore.

DR. GOLDMAN: Okay, so that's food for thought.

DR. MOURE-ERASO: Now as having been part of the process, I, I think that I did find especially with the advent of the Internet and the web sites that a very rich way of understanding how were the reactions of the, of the Board of Scientific Counselors to the decisions of the RG1 and RG2 appear in the discussions that are printed in the, in the minutes of the meeting of...so, so there is a record of the reasons why there might be sometimes a divergency of, of, of, of recommendations, and as you said in your, in your... is like there are three separate recommendations with the reasons that are given in detail in the minutes of the discussions. So, for anybody that want to know the process by which the final decision came, you can see that it might be that the RG1, RG2 and the Board of

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Scientific Counselors' recommendations are different and, and, and the reasons why could be getting out of the minutes of the meetings.

MS. FELTER: Susan Felter. I have a, a clarifying question. Is it possible to put the slide back up for one second?

DR. JAMESON: This one?

MS. FELTER: Right. In, on the right hand column it says that these are three independent recommendations, and my question is whether the commentaries that are provided by the RG1, you know, appears to be sequential. If those are written up and appended to the document, are those available to the RG2 before they start their review so that in fact and, and those together then are all available to the Board of Scientific... so, so that is in fact a sequential.

DR. JAMESON: Yes, as, as, as we proceed through the process...

MS. FELTER: Okay.

DR. JAMESON: ...when, when

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the RG1 completes its review and makes its recommendation there is a summary of the recommendation that is prepared, which includes the vote for, of the rec..., of the recommendation and that information is published on the web as soon as it's available, it becomes part of the public record and, and forwarded on to the, to the, to the next review committee so that they have that information. And, and the same is true for the RG2, as soon as they finish theirs and, and make their recommendation, a summary of their review and recommendation is prepared, placed on the web and, and forwarded on as part of the package to the RoC subcommittee, as are all the public comments we've received all along this process. I mean, we.. when we put out a Federal Register Notice and, and say we, we're soliciting public comment and, and we ask that you get your comments in in 60 days, we put a deadline on there only that we can guarantee, that if you get us information within, by that 60 days, say for example, we can guarantee that we will get

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that information in the package to the next review group or to whatever the next step in the review process is. That does not mean that after 60 days we will not accept comments, that is not the case. We will accept comments on, on what we're doing at any time. We're very, very happy to receive comments, but we put a deadline only so that we can guarantee you that if we get it by that time we can include it in the package with the next proc... with the next step in the process.

DR. GOLDMAN: Okay, yes.

DR. ALLABEN: I'd like to make one comment. Having been involved with the RG2 and the Executive Committee and, and been around long enough to evaluate documents that sort of evolved as they went through the review groups and changed to the Executive Committee and then also seen where they've been stagnant, it's sort of you're damned if you do and you're damned if you don't, but I think that when the document changed over time and then it got to the Executive Committee meeting, often they would

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look back at RG1 and RG2 and try to determine why they voted in a particular way, and it could be confusing because they wouldn't understand that, that RG1 and RG2 didn't have a particular set of information. And if it was just sort of melded into the document it would be less clear. But by having the same document, for example, the Executive Committee can look back and see what document RG1 and RG2 looked like, looked at, then they can also see how additional information was added and impacted the subsequent decisions, and so I think the present format is probably the best at this time.

DR. GOLDMAN: Okay, well, yes. Chris.

DR. PORTIER: I just want to reenforce what Mark pointed out, and that's one of my concerns and the Director of NIEHS's concerns as well and now with the process we're trying to put into place here, the Director will be able to sit down, evaluate the evidence, understand hopefully everyone's point of view and how they

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received, how they got to that point of view and make a decision that's informed rather than potentially hidden in some oth...in some way. We're trying to make it as open and as clear to the point of the Director can actually see the evidence in front of him about what the scientific review was like, who said what, why, and make a, hopefully an informed scientific decision from that process. And to comment on the independent review groups obviously, that was your question about the word independent, in this case the word independent simply implies that they're different people on the different groups. They are not necessarily independent since obviously the decision of one is portrayed to the other.

DR. GOLDMAN: Thank you for that and thank you, thank you, Bill, for that presentation. I think that it's clear that there is a lot of openness to change here, that things have changed and are continuing to change in the approach that has been taken to make sure that people can have as much access to the process as

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possible. I'm going to now take the prerogative of the chair, break the order of the speaker's list just a little bit because I know that Dr. Goldstein has a plane to catch and the weather is pretty dicey out there, so Bernie, if you want to come forward and give your, your comments.

DR. GOLDSTEIN: Thank you, Lynn, I really appreciate that. The, it's particularly important on a day when the planes are down and delayed but you never know. You heard Bill Jameson and the very last point he made about changes talked about working with regulatory agencies to help get the message. I think more has to be done there. What I am particularly concerned about is the fact that as Rafael Moure-Eraso just told us, you've got a public health decision here, there's a, if you're listing something as something that causes cancer you've got to really act on it. At the same token, we've heard, I think very compelling information from industry sources about certain things that get listed, appropriately so in my view, as carcinogens

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having second order and third order effects. Sometimes the effects are on the industry of welding, sometimes they're on public health as perhaps the Tamoxifen example, there are others. And it seems to me that the criticism is really not appropriate toward the NIEHS who had a hazard identification process. It's really appropriate toward the regulatory agencies themselves. This process, relatively uniquely I'm told, for all the processes worldwide, has the regulatory agency sitting in on at the very beginning and they are there throughout. And there's absolutely no reason that they should not be able to decide in advance what they will do preliminarily at least about the decision. So what I would suggest as a very formal part of the process would be something in which every one of the regulatory agencies would be required to provide, I gave it an abbreviation and a name because after all this is the way we work. I gave it a three letter abbreviation because four letter abbreviations don't work well in Washington in my experience, but basically it's, it's

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the regulatory agencies who are involved in the NTP process, they ought to say what they plan to do about it. And they ought to be working at an issue as soon as something gets put on the nomination list. And they ought to release this all at the RoC listing or de-listing or in the situation of something like Tamoxifen we ought to release it not then which is what happened at that point, but when the Board, when this thing gets to be public which is long before it formally does come out through the Secretary. And they ought to basically be able to say what they think is important. And, you know, I'm not talking about something that's binding, I'm talking about a non-binding preliminary intent of an agency to review data, to gather data, to begin its regulatory process or say in the case of Tamoxifen, as the Consumer Product Safety Commission is saying basically, not part of our mission. Now a lot of these things can be looked at from the point of view of an agency that needs to basically be responsive including what its time frames are going to

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be. In other words tell the public flat out what you expect to be, to be done here, it gives you an opportunity to make a public health statement if need be. Don't worry about whatever the compound is, it may have some benefits or that this is related specifically to a particular situation. The, the bias I'm coming from, just so that everybody knows what the biases are, is I performed research and development at EPA lo these many years ago and always in a regulatory agency there is a problem of getting the scientific information from the scientists involved in the agency who are very often involved in these processes and the folks who do the regulation. Well, let's force that issue, let's make sure there is a rapid response, let's make sure that every time one of these decisions are made, the agencies involved that have been involved from the get go are able to say, what is it they plan to do about it. Now the plan, as I say, may be just simply, simply a matter of saying that they're going to gather information, could be on Tamoxifen

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to point out that they are I think still in the process of gathering information about drugs that get into, that humans use and it's free to get into the worst kind, what does that do? So there's a reason for them to add perhaps Tamoxifen to that list, at least to look at it. Again, notify the public as to what they plan to do and when they should plan to do it, and we're talking about, I'm talking about something that if it goes more than one paragraph, it's probably going too long. We're really just talking about a short informational package of what the agency intends to do about this, and I see no reason that that can't come out just as part of the, of, of the record at the same time everything else as we raised. I, I'd point out to you that a lot of the comments that are made here, particularly from folks from industry, really ought to be made to the regulatory people, they're the people who are accustomed to responding to it, they understand the process better, what's going to come out of it. It's not the kind of thing that you really, really

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want your, your scientists to be responding to, you really want your regulators to be responding to it, and sometimes the important thing to you is that they respond early. And again the attempt here is to just simply put on record to every regulatory agency that's part of this process from the very beginning, that they will have to respond and if they're going to respond it's in the public benefit, the industries' benefit that they respond more rapidly rather than slowly. That's my suggestion.

DR. GOLDMAN: All right. Let me see if any others have questions or comments. Yes, Mark.

DR. ALLABEN: NIOSH is not a regulatory agency but I always think in terms of how we might answer this question and how would you think that these agencies would give you something beside a boiler plate answer for every listing, in other words, if we looked at this and knew that when something was listed as a known or reasonably anticipated, we would say, in those particular cases we do this, this is

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on carcinogens. What would you expect you might get beyond that?

DR. GOLDSTEIN: Well, we were saying like Nickel Steel, the industry, basically stainless steel is saying that they are going to be hurt by this issue of people not buying stainless steel because they think that it's a carcinogen, I'm not sure that that's correct but it's just what they report. But I think if, if you really are going to find Nickel as a problem then one of the Nickel Steel issues has to do with people working Nickel Steel, working in stainless steel, grinding it or otherwise and if NIOSH wants to say or OSHA wants to say that in 90 days we're going to gather information as to whether there is exposure during the grinding or other processing of Nickel Steel, you are basically committing yourself to do something within sometime. Now it's a non-binding commitment but it is something which you've probably looked at and you've said, well, gee, they're now saying Nickel is a carcinogen, Nickel Steel, I wonder if there's any exposure to people who

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work in this, the people who repair it, people who are tearing down old buildings with Nickel Steel sink, sinks, and so we're going to look at this and we expect in 90 days to have that information to understand whether or not it's a major risk. Now that's the kind of thing that I think can be done, should be done.

DR. GOLDMAN: That's a brilliant idea actually, that maybe if the agencies came up with boiler plate language for that, then they might actually have some policies that would be clear, that wouldn't be a bad thing. So maybe that would be better, actually, but that has nothing to do with, of course, what the National Toxicology Program would do, but it.. you know, it's not a new idea either, remembering the old OSHA carcinogen policy and what Eulah Bingham did years back, you know, it doesn't hurt to have some idea of what you're going to do if something's listed. I, I don't think that the agencies have that kind of policy, most of them, that, you know, that oh, god, if there's a new listing and it's under my

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they, they thought that through, it probably would be a good thing if they would. I just had a trivial suggestion which is that you would call it an advanced notice instead of a preliminary notice. I, I think in some ways it's a good idea, I'm confused about what the timing should be though, Bernie, I mean, I think it could be, because just at the point of, you know, many things that are nominated and considered then end up not being listed. So, it could create confusion if the agencies were to publish some notice, that then would not come to fruition because it didn't end up being listed, so, but, so that would need to be kind of worked through, but I don't think it's a bad idea.

DR. GOLDSTEIN: Maybe the agency should have an idea though like if it is listed as a known we'll do this, if it's not listed we'll do that, I mean it's just...

DR. GOLDMAN: Some policies would be great, that's, it's really, that's really a good point, and it does create a lot of uncertainty for the community, the

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fact that there, there aren't those guidelines that are in place. Any other comments or questions for Dr. Goldstein before he runs to the airport? Yes.

MS. LE HURAY: Just two things naturally, this is Ann Le Huray again, one is just to point out it's not NTP's fault that there's a number of regulatory triggers that are just automatically triggered, written into the regulation, one being an OSHA trigger if you have a finding of carcinogenicity and the other being of course the Prop 65 in California trigger because NTP is recognized as an authoritative body, and the, and the second I just would like to say about... that it's not the kind of thing that, I think you're quite right that you don't want to have your scientists necessarily making policy decisions, but the chemical industry being a science based industry, we would like to have our scientists engaged as well and that's, that's part of... you know, some of the root of the frustration at least of, of industry comments about getting engagement

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because we think we have pretty good scientists and you know, well, we think that they know quite a bit about the materials that are being listed, so one of the frustrations is that our scientists would like to be involved and, and engaged in the process as well, so.

DR. GOLDMAN: I'm going to take one last comment here and then move on.

DR. CARPENTER: As a scientist who works in an agency that deals heavily in policy, I have some reservations about what you've presented. I think NTP, as I perceive this process is, is that it is a scientific process, that all attempts are made to keep it free from policy until the very end of the process and I think that's actually a good move, again speaking scientifically, because you really don't want policy to drive your science until the appropriate time. And I wonder whether policy implications being taken into account by a group of scientists considering what should be a scientific document, scientific decision is, is a correct move.

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DR. GOLDSTEIN: I agree with you completely and I'm sorry if I, if my presentation was too quick to make that point. No, I think that elsewhere within the agency there ought to be people being told by their scientists that this is coming forward to a decision, it could be a known, it could be a reasonably anticipated. We need to prepare what ought to be done, but that's your job, the regulators, to decide what it is that you think we ought to be saying about this if it turns out to be known, about what we plan to do.

DR. GOLDMAN: You were not suggesting that the risk assessors would do this?

DR. GOLDSTEIN: No, I don't, I don't suggest this to the NTP that the risk assessors do this, what I'm suggesting is that when this gets published each of the agencies that should've known about this from the beginning because they've been sitting at the table basically have their regulators come out and say here's what we intend to do.

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DR. GOLDMAN: Okay, thank you very much. Next up on the list is Donald Smith from the UVIR Research Institute. My understanding is that he was not going to be able to make it today. Is that correct? And I, I have before me a written version of his testimony which I suppose I could just read it into the record, see if I can, if I can find it, and you'll have to use your imagination and pretend that I'm Donald L. Smith. I'm not even sure I can remember what he looks like. I think we have seen him here before. Good morning, my name is Donald L. Smith and I am the Director of Research at the UVIR Research Institute in Tucson, Arizona, an organization studying the biological effects of ultraviolet visible and infrared electromagnetic radiation. It is my opinion that the primary weakness of the Report on Carcinogens is that it errs fundamentally when (a) it relies upon the outmoded and scientifically unsupportable Linear Non-Threshold Haz..., LNT, hazard assessment method, which assumes that because an agent, substance or mixture, ASM, is

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hazardous at a specific dose, it is hazardous at any other dose, for evaluating potential listings; (b) it fails to mention the beneficial effects of an agent, substance or mixture, ASM, when that ASM has both beneficial and harmful effects and this failure is especially misleading and potentially damaging to the American public when the ASM, like for example, ultraviolet radiation is essential for survival of life on earth. It is wholly irresponsible for any federal scientific body, NTP, and quasi-health agency, NIEHS to omit from a document, the RoC, purporting to assess the harmful effect or effects of an ASM on the human body, a detailed discussion of the beneficial effect or effects of the ASM on the human body when the ASM is known to have both harmful and beneficial effects. Thus if the RoC is to warn the American public accurately about the health implications of an ASM that has both beneficial and harmful effects like ultraviolet radiation, it must be sure not only to warn them about the harmful effects of the ASM, but also to

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the ASM. To do otherwise renders the RoC incomplete and misleading because it will not equally and fairly present both sides of the risks involved to the American public. And that is the, the end of, of Donald L. Smith's comments, and those will be, have now been read into the record. Why don't we move to the next, the next commentor if that's okay with everyone, who is Timothy French from the Engine Manufacturers Association. Are you here? Okay, not being present, I'm going to move forward. If people arrive late we will fit them in at the end, and so next is William Kelly from the Center for Regulatory Effectiveness, speaker #4.

MR. KELLY: Do you want me to come up there or speak from....

DR. GOLDMAN: I think it would be probably easier, but if you'd rather speak from back there, it's fine but. Why don't you, why don't you come forward, I think it might be easier for those of us up here certainly to see you.

MR. KELLY: So I'm speaking

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to your faces, not to your backs.

DR. GOLDMAN: Exactly.

MR. KELLY: I'm not sure whose this is, but... We submitted detailed written comments which are available outside, I noticed there are some, there were some formatting problems in posting them electronically, so I have better copies if anybody wants, wants one. Really the only change was made in them was the number of some of the recommendations at the end. And I see that one of our, our major recommendations, I believe has been taken care of now and that was the recommendation to be sure to, to set a definite time for the release of the background document and I'm, I'm very pleased to hear that commitment is being made to release that before the RG...RG1, with a fairly specific time frame before the RG1. We think that the nomination review committee is a, is a very good idea and I guess the, the main remaining recommendation we have centers around that. With the institution of that new committee, it in effect moves the, what

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I would call the point of no return farther forward in the process, whereas previously the RG1 was the one to determine the sufficiency of the nomination, we now have a new group before the RG1 making the basic, preparing the nomination background and submitting it to the Director for approval and then the review process begins. In view of this, I feel even more strongly that once a nomination is submitted and is intended to be submitted to the nomination review committee, that is when there should be a public notice and an invitation for public comment to the nomination review committee. And the purpose of this is not to, to argue about whether a listing is appropriate or not, it's just to make sure that the nomination review committee is really, has available all the significant information it needs and this is particularly important with what I would call mixed exposures or non homogeneous exposures. There are a lot of exposures in the areas of worker exposure and things like industrial minerals and metals where you don't have a synthetic

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chemical that's a very clearly defined substance. In fact, in the case of say an industrial mineral, the, the actual exposure may differ from one mine to another quite dramatically as we, we've seen in some of the reviews. In other cases where you have worker exposure, the types of exposure, different types of facilities may be different, that workers may be exposed to, to co-carcinogens, or different sub.... substances, some of them also potential carcinogens along with the substance under review, and the nom... the people on the nomination review committee aren't necessarily going to be aware of those very site specific types of issues or mineral or compound specific issues. And the nomination review committee of course can review the available peer review literature, but as people may have noticed, it, in the issue, with regard to the issues of exposure and how the substance is actually defined, those two parts of the background document are not dependent on peer reviewed literature. The committees are free to consider other sources

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of information. So I think it would be very valuable to let the public and stakeholders know when a nomination is going to be under consideration and wheth..., when the nom..., it is going to go to the nomination review committee so that they can suggest points that need to be considered, provide information particularly on, on these kinds of issues of what exactly are the physical chemical characteristics of a compound, what the exposures are, not quantitatively so much as qualitatively and how they might differ from, from site to site. And also to recommend at that time people who might be spe..., very knowledgeable on these types of issues and those might be, they're not necessarily published authors, but they might be, for example, health and safe... safety experts at a particular company or even a mine operator who, or a mineralogist who is familiar with that particular type of compound at a particular mine or a particular facility, but has not necessarily published a paper on it. Okay, so that's, that's the next major recommendation that we

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had after releasing the background document before RG1. Of course we've recommended that since this is now an evolving process with there really being not just a background document, but a bet..., what I would call a background document package, as it moves forward through the process, each committee adds comments and recommendations to become part of the package, that information be posted as it, as it develops and before each review committee meeting so that people have a chance to see it and if they, they notice anything that's really off in there they have a chance to comment to the next committee. Now what..., probably the most radical suggestion we made which has been referred here today, not necessarily attributed to us, is, is the role, has to do with the role of the NTP Executive Committee. We actually... we made the point that, that that is often viewed and in fact is more properly characterized as a policy level type of committee rather than a scientific review committee. As I understand it, even though those meetings are

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confidential we have gotten some reports on, on how they're conducted. Those...the Executive Committee does not necessarily get into the details of a particular proposed listing the way the other review committees do. They will look at, you know, what has happened in the review process, did RG1 and RG2 differ from, in their votes from each other, and did they differ from the RoC subcommittee and what are we going to do about that, or what are we going to do about the Tamoxifen issue, but they don't get into the science so much. So the question and I'm not.. we have proposed that they actually be removed from the review process, or as has been suggested today perhaps their role should just be clarified more, but I would suggest, certainly they have a place in the process. I mean they're participating agencies, it's an NTP listing, it's not an NIEHS listing. Dr. Olden is Director of the NTP which means he works with all of these other agencies, he's not the guy who runs these other agencies and that will be true of any subsequent Director also of course.

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So there's a place for it, the Executive Committee, but I think it would be more constructive for the process if instead of having the Executive Committee actually vote on a recommendation, which I think they have mostly in the past, though I have no way of really verifying that, that the better way to do it would be to let each of the agencies as an agency submit comments to the Directors and of course they would go through the head of the agency or whoever was on the NTP Executive Committee before they got to the Director I assume and they'd be signed off on. But then the agency would be freer to have, you know, their best scientists, their most qualified scientists, particularly with regard to a particular proposed listing, take a look at what had been done with that listing and, and submit really scientific comments to the Director and the Secretary. There have been other issues raised today which I think will come up in the discussion, so I'm going to cut it short and not comment on those yet. I may.... well, you can count on me to jump in

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as they come up in the, during the rest of the discussion. So that's all I have for now other than what's in the written comments we submitted.

DR. GOLDMAN: Thank you very much for that. Are there questions that people have, or points where you would like to receive clarification? Mark?

DR. TORAASON: Yeah. Playing a role in the Executive Committee not as a, as a member but as a, sort of a briefer for our Director I would argue that I think that at times the Executive Committee can be more technical than it's being placed here. What, what does not take place at the Executive Committee from my perspective is a rehashing of issues where there's a great deal of agreement. It's only in particular cases where there's a contention over an issue and in these cases the Executive Committee will evaluate it. So I think that their vote is important and they do play an impact and in a sense... I can't speak for all the agencies that are involved... that the Director doesn't go... our Director doesn't

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go to the Executive Committee meeting without a thorough review of all the material and a brief on that material, so it's just that if there's nothing in contention then it's not...

DR. GOLDMAN: Yeah.

DR. TORAASON: ...brought up and discussed again.

DR. GOLDMAN: Thanks for that clarification. Are there questions or..... yes, Dr. Moure.

DR. MOURE-ERASO: On the issue of, of the nomination committee that you were, you were discussing in there. The way I read it you are saying that or imply that the party that nominates a chemical from the NTP to be considered presents evidence or presents the literature of the, of the, of the chemical while you are making the nomination. My understanding, and I wish if that NTP people should comment on this is that, the responsibility of gathering the information for the nomination is the NTP...., I mean they, they have, my understanding is that they have facilitated

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the process of nomination that anybody that consider that something should be nominated should be free to present it and then within the NTP, the gathering of information occur and the decision is made if it, it is there something, if there is enough material to do it. But, I, I, I would like to, to, I wonder if you are suggesting that a nomination be made more formal and that the people that nominate present evidence?

MR. KELLY: My understanding of the process as it's written up right now is that, is that the nomination review committee is free to supplement what was submitted by the.. along with the original nomination. The point I'm making is that I think it's important for the public and stakeholders to know when a nomination has been submitted and when there is going to be work done by the nomination review committee in making a recommendation on the sufficiency of the nomination and gathering further information. And it's the gathering further information part that I was particularly interested in. I..., once they make that

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recommendation and the Director approves it, the process is set in place that you have to go through almost a two year review process and it's a shame to see that happen if the nomination has not been based on complete data or on data which is somehow flawed. So I would argue that it's important for people to know the nomination is about to be considered and to get to the nomination review committee all available information. I think it's especially important and to suggest individual experts that that committee should consult for further information, particularly on issues they regard as especially significant. Does that...

DR. MOURE-ERASO: Yeah, I understand better what you're saying.

SPEAKER: I must be missing something, Bill, how is what you described different than what he is requesting? I mean you, you, you said you are going to solicit comment before the review begins, aren't you?

DR. ALLABEN: Yeah, we, we

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for a nomination begins, but I think what Mr. Kelly is suggesting is before we even identify the nomination, before the nomination committee sees what is being proposed for possible nominations for listing that there be a public notification of what we're even thinking about considering and getting some input on that, is that...

MR. KELLY: Well, there are really two distinct parts to the process now, that the review process does not begin until the nomination which has been approved for sufficiency goes to RG1, and the public announcement is not made currently until just before the RG1 meeting. What I'm suggesting is that the public announcement process needs to be moved farther back to the point where prior to consideration of the nomination by the nomination review committee so that they are sure that they have all the important information on that substance or exposure. Does that, does that help, Mark?

DR. GOLDMAN: Chris, did you want to chime in, I think I understand what you're saying, I actually...

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DR. PORTIER: I, I understand. I understand what you're saying and I want to make a few things clear. Number 1 is that the policy of the National Toxicology Program is that just because a chemical enters the review process does not mean in any way, shape or form it is suspect as a carcinogen; that is not the intent of our process in advance. Obviously we spend time and effort up front looking at what's available to us, we balance a lot of issues in the nom..., in evaluating what the nomination committee gives us in terms of resources we have available to include in our overall review and a number of things. And so it's not simply a science issue per se up front. But I do want to make it clear, you're presuming in some sense we're reviewing this in the nomination committee with the intent of deciding whether it has enough evidence to actually make the listing, that's not the intent. The intent of the nomination committee is to decide whether or not there is enough evidence to review, not enough.. not the question of whether that

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evidence points in a, in a particular direction or not. I will also point out that in the review process that Bill outlined, once the Director has selected a list of compounds that we can reasonably review in a two year period in the NTP for the Report on Carcinogens, you have the opportunity to comment on those nominated chemicals and clarify the record of the science on those chemicals which we do encourage you to do, and you have the opportunity at that point to suggest experts who we might include in the overall evalu... preparation of the background documents because at that point we have not started the background documents. So there is an opportunity to do effectively the same thing you're asking for after the choice has been made that these are the things we will review.

MR. KELLY: I would like to see specifically stated in the procedures that before the RG1 review, the invitation for public comment will include the invitation for recommendations on experts who should be included in the preparation of the

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background document. I believe that's not stated explicitly in the procedures right now. And I understand your point of view, I am sticking with my point of view that it, it would be valuable for the nomination review committee to, to have a chance to review all the best available information before they make a decision on whether to go forward with the nomination, and as I said I understand your point of view also, that that's not a, it's not a review decision, so there we leave it, it's a suggestion.

DR. GOLDMAN: I have a question for you. You suggested in your, in your statement that it would be good to expand the core of knowledgeable experts to include people who are not scientists and don't have any scientific information to contribute about the carcinogenicity of the chemicals like mine operators and you listed some others and... I was very surprised at that suggestion and, and I wanted to understand what it is that you felt that those folks could contribute to this kind of process in terms of trying to sort through

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evidence about carcinogenicity?
MR. KELLY: Well, I'm not sure I meant to suggest they weren't scientists. I mean some of them might be, might be...
DR. GOLDMAN: You said they might not have published...
MR. KELLY: ...be a min..., be a mineralogist, for example.
DR. GOLDMAN: Uh-huh. (Indicating affirmatively.)
MR. KELLY: I don't know whether you'd consider that a scientist or not, but say somebody who runs a mine and analyzes samples from the mine or whatever would be in a position to say what are the actual exposures at that particular mine and the same would be true for say a production facility...
DR. GOLDMAN: Is what you're getting at...
MR. KELLY: Those are the technical, technical people but not necessarily scientists in the sense of being toxicologists or epidemiologists or

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pathologists.
DR. GOLDMAN: So is what you're getting at is just physically what or chemically what's the actual identity of the agent? Is that the issue you're trying to get at, is there a scientific issue in there about, you know, mineralogy or chemistry of the agent?
MR. KELLY: Yes, we're talking, we're talking...
DR. GOLDMAN: Is that what...
MR. KELLY: ...about the properties...
DR. GOLDMAN: 'Cause I just didn't...
MR. KELLY: ...properties of the exposure, whether it's a single exposure, whether it's a mixed exposure, what exactly it, it looks like. Some, particularly industrial minerals exist in a, quite a variety of forms depending on the particular mineral deposit. Some of you may be familiar with the, the whole controversy having to do with, I forget the, the Vermiculite controversy and whether...

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DR. GOLDMAN: The question of what is Vermiculite.
MR. KELLY: What is Vermiculite, does it have asbestos in it or not and you're going to need people to present technical information from the Libby facilities itself, you know, presumably there is exposure information that has not necessarily been gathered by toxicologists or epidemiologists or pathologists or, or other...
DR. GOLDMAN: Okay, that helps me understand.
MR. KELLY: ...health sci..., health scientists...
DR. GOLDMAN: That helps me understand what you meant.
MR. KELLY: ...that will help, help understand what exactly is the substance to which these people are exposed.
DR. GOLDMAN: Thank you very much. Okay, well, I've let us go past our time for the break and.....Oh, one more comment, sorry.
DR. DELZELL: I believe you

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mentioned that the, the language of the solicitation for public comments that's made after the nomination is, is not clear. Can you be more specific about that?
MR. KELLY: You might be referring to the comment I almost directed directly to Chris that the, the currently the solici.. solicitations for public comment do not ask the public to suggest compound specific experts who could contribute to preparation of the background document and I suggested that that be specifically included in the notices and in the procedures. Is that what you're referring to?
DR. DELZELL: Yes.
MR. KELLY: Did, am I clear about that?
DR. DELZELL: Yes.
MR. KELLY: Okay. Dr. Toraason, I got the feeling I did not satisfy...
DR. TORAASON: No, I understand it now. As we went around and around there, we talked about it.
DR. GOLDMAN: He understands.

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DR. TORAASON: Yeah, I understand.
DR. GOLDMAN: Understand the...yeah, that's important, thank you so much. Okay, as I said before, I was starting to say we did go right through the break and what I want to propose is that we would continue in this manner until noon and break at noon, for a brief lunch. Is that okay or do we need to adhere to the 12:15 break time? Mary, just pipe up if...it's, that's okay, is that okay with people in the audience that instead of at 12:15 we would take our lunch break at 12, so that I'm, I'm basically cutting out the little morning break, but trusting that you can come in and out. So why don't we go ahead and keep moving on? Is James McGraw here?
MS. LE HURAY: No.
DR. GOLDMAN: No, I'd heard...yeah, I thought he wasn't going to be able to make it, but we do have a letter from him and I.. and Richard Becker I take it is still digging...
MS. LE HURAY: Through the

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me his slides.
DR. GOLDMAN: Or is he going to continue to try to soldier on and get here, they might dig him out if he wants to go later. I could move on to the next speaker.
MS. LE HURAY: I, I could either give his presentation, or if you're going to continue tomorrow, he doesn't think he'll be able to get out today.
DR. GOLDMAN: We may be concluding today, so it could be that the best thing then would be to go ahead and let you keep your place in line here and, but they may be plowing the area out. If, if...
MS. LE HURAY: Well, I know there was some areas, and I'm not sure where Rick lives, but for example they closed Georgetown Pike this morning because of ice.
DR. GOLDMAN: Yeah.
MS. LE HURAY: So if he lived out that way it's more, more than a plowing problem, it's ice on the road, so...
DR. GOLDMAN: Okay. I know. I drove here, I know about the ice, okay,

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let's go ahead then and...
DR. PORTIER: Clearly we can wait 'til after lunch for your presentation and you can contact him and...
DR. GOLDMAN: And...
DR. PORTIER: ...discuss the issue...
DR. GOLDMAN: Also I have a re...
DR. PORTIER: ...we can decide after lunch.
DR. GOLDMAN: I also have a request from one of the later speakers to go before lunch, if.... is that.. would that be okay for you to stay through lunch and...
MS. LE HURAY: Sure, that'd be fine.
DR. GOLDMAN: ...do it after lunch? Is that all right? Okay, why don't, why don't we go ahead then? Jennifer Sass had requested to try to go before lunch because of a scheduling conflict. So we will then accommodate that and.... I'd like to see Rick here so let's call him.
MS. SASS: Is it okay if I

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give my comments from here?
DR. GOLDMAN: I think it may be difficult, if you, if you do need to speak from back there, there is a mic on the pole, you could use that mic I think or sit down at your chair, but then we won't be able to see you, so it would be better if you're speaking into a mic and we are recording so we want to make sure that...
MS. SASS: Is this on? I'm Jennifer Sass with the Natural Resources Defense Council. These are short comments and I've also handed a few copies in some written comments... some written copies. I have only two points and I, I don't think they're, they're actually very radical at all, so I'm sure that when you hear them you'll really be excited about making these minor changes. I'm also volunteering, I, I train guide dogs, this one's in training, so I hope she doesn't get out of hand. The first is the criteria I think need an explicit description of how mechanistic data can be used to upgrade an agent. The NTP criteria for listing agents in the Report on

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Carcinogens as quote, known to be human carcinogen, unquote, requires sufficient evidence of carcinogenicity from studies in humans, which indicate a causal relationship between exposure to the agent, substance or mixture and human cancer, that's the criteria as it's listed. The criteria also allow for conclusions of carcinogenicity to be based on scientific judgment with consideration of all relevant information, this is also written. This relevant information may include mechanism of action information. The criteria, the criteria describe how mechanistic data may be used to de-list or downgrade an agent that causes cancer in animals. The criteria state, quote, for example, there may be a substance for which there's evidence of carcinogenicity in laboratory animals, but there are compelling data indicating that the agent acts through mechanisms which do not operate in humans and would therefore not reasonably be anticipated to cause cancer in humans, that's the language of the example that's given. However, it is an obvious, obvious absence

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that the criteria lack an explicit description of how mechanistic data can be used to upgrade an agent. Especially to the known human carcinogen category. So, we think that it's essential to have explicit criteria laid out that would allow the use of mechanistic data to list or upgrade an agent to known human carcinogen where it's appropriate. I know that the NTP considers this, but I think it should be part of the language and not just a, a negative example. My second point is that the NTP Report on Carcinogen needs to maximize the appropriate use of mechanistic data to properly inform the public of cancer hazards that they may encounter in the environment or the workplace. After presenting the criteria, the report provides a definition of human studies as traditional cancer epidemiology, data from clinical studies and/or data derived from the study of tissues of humans exposed to the substance in questions and useful for evaluating whether a relevant cancer mechanism is operating in hum.... in people, that's the language that's used. This

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clarification should be part of the criteria as opposed to listed below and even this clarification though, we don't think is sufficient, for example Vinyl Chloride is a known human carcinogen, but Vinyl Bromide and Vinyl Fluoride also produce tumors in experimental animals and the same types of DNA adducts in exposed animals and the same metabolites by rodent and human liver microsomes. All of this information indicates that these Vinyl halides act by a common mechanism and should be regarded as human carcinogens. I think that the NTP does take this kind of thing into account, I just think that this spe..., the language should be explicit and it should be included in the criteria. It would be misleading for a worker to believe that his or her cancer risk is reduced when working with Vinyl Bromide for instance versus Vinyl Chloride. The NTP RoC needs to maximize the appropriate use of this mechanistic data to properly inform the public of cancer hazards that they may encounter in environments and work places by including specific and

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explicit language in the criteria, thank you.

DR. GOLDMAN: Any questions for Dr. Sass? Comments?

DR. MOURE-ERASO: I appreciate your comments Dr. Sass, I think it's a, it's a topic very near to my heart because I was involved in these decisions and, and I would like simply to add that, that the first part of your, of your comments that, that you say, that an example is, is, is put on the current comments on the criteria that of how mechanisms of actions could be used to change a nomination or, or a, or a decision of being a known human carcinogen to being a reasonably expected to be a human carcinogen. Actually the, the, the cases of Vinyl Chloride, Vinyl Bromide and Vinyl Fluoride is probably the counter example that is the opposite in which mechanism data was considered in the discussions of the bureau of scientific, of the, of the Board of Scientific Counselors to, to change the nomination for reasonably expected to be a carcinogen to a known carcinogen, and actually the decision of the

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Board of Scientific Counselors was specifically that based on the similarities of action between Vinyl Chloride and Vinyl Bromide and Vinyl Fluoride; so there is a particular example of what you are saying in the first paragraph.

MS. SASS: Right, thank you. Yeah, that, that is true of course and what I'm hoping is that tho..., that kind of language and some language that captures those kinds of uses can be put into the criteria more explicitly.

DR. GOLDMAN: Okay, don't everybody stampede toward the door, but I've had another request for somebody to be moved up in the order and which we're going to go ahead and accommodate, another flight that somebody has to catch, and so speaker number 8, Dr. Roth.

DR. ROTH: Thank you for accommodating me, I, I don't know if the flight's going to take off after hearing that Old Georgetown Road was closed, but... I have been involved with beryllium for over 25 years as a U.S. government agency

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official reviewing the beryllium epidemiology data, as it was at the time. As a researcher I've published quite a lot on the epidemiology of beryllium. I was a commentator to a number of different panels and committees such as this for OSHA, EPA, NIOSH and then I served on numerous panels, agency panels to deal with beryllium. My full comments on the beryllium hearings, the NTP beryllium hearings are, was submitted to you and they're available outside as well. I would just like to summarize some of these comments here in about five or ten minutes. The comments are divided into two portions, the first of which is the process, and the second I'd like to give you a little bit of the technical substance. The major problems that we've had with the process section of the beryllium hearings with NTP are (1) NTP did not prepare an adequate background document, (2) They did not provide the public time to review the background document, (3) They did not give the Board of Scientific Counselors sufficient time to review the background document and the public

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comments, (4) They did not give the public sufficient time to address the Board of Scientific Counselors, (5) And they did not permit dialogue or questions and answers between the public and the Board of Scientific Counselors, and finally they did not provide a response to comments that were submitted and some of these were pretty technical comments that would have made a substantial difference in the Board's decision about the carcinogenicity of beryllium. To give you some specifics about the process, the public was not given an adequate opportunity to present their comments to the NTP. One deficiency was the scheduling of nine chemicals to be reviewed by the Board of Scientific Counselors during a two day period. During public comments on the beryllium nomination, members remarked at several points as to the need to conclude consideration of beryllium and move on to the remaining chemicals because of the press of time. Another deficiency was the limitations on the interaction between public commentors and the Board of Scientific

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Counselors in discussing the adequacy of the two key studies. Indeed at various points some members of the Board of Scientific Counselors agonized as to whether they should even be discussing the comments from the public or answering questions as opposed to merely listening, listing the comments. Next the composition of the Board of Scientific Counselors was another deficiency; only seven of the twelve Board members were present for the deliberation, five of the members did not hear the public comments including some principal reviewers. In fact, the key with beryllium epidemiology is the epidemiology and there was only one epidemiologist present at the time. Another deficiency was selecting as one of the three primary reviewers a member who had co-authored at least two papers and was apparently working on a third paper with Dr. Ward. That was one of the key epidemiologists. This person's work was at the crux of the board's decision to support a cancer classification change for beryllium. Persons should not be chosen as primary reviewers on proposed nomination for

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a change in cancer classification if they have been professionally close or personally linked to an author of the primary studies used to support the change. Those summarize some of the problems with the process. NTP's criteria for listing states: conclusions regarding carcinogenicity in humans or experimental animals are based on scientific judgment with consideration given to all relevant information. In several respects, relevant information concerning beryllium was excluded from consideration by NTP. And there were two instances of this. One was a Ph.D. thesis whose document was available online and they refused to consider it because it was just a Ph.D. thesis and another of which was a paper that I had published with Levy and Roth. The, an early draft of the paper was submitted to the committee, they refused to look at it because it wasn't yet peer reviewed, but it was peer reviewed and published two months before the background document came out. So that data were available. And the data in the paper were key because they addressed just the issues

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that were raised at the meeting, and the key issues was, smoking was one of them and our paper had shown that adjusting for smoking alone would have changed all the statistically significant associations with beryllium and lung cancer would have been attributed to smoking alone, so smoking was a critical issue. Another critical issue in the paper was whether or not to compare the lung cancer rates of beryllium workers compared to the U.S. as a whole or to compare it for the relevant rates to the city in which the plants were located and in which most of the beryllium workers worked. Adjusting for city rates instead of using national rates, which include rural areas where lung cancer rates are much lower, would have also changed the association from beryllium and lung cancer from being positive to being negative, no association whatsoever. To put the, all the beryllium data into perspective is that all these papers, ours as well as all the others, looked at seven beryllium plants in the United States, the, all the production facilities in the United

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States. Of these, five showed no statistical association between lung cancer and, and exposure to beryllium whatsoever, none whatsoever. In fact some of these five studies had a negative association, that is to say for the beryllium workers the levels of lung cancer were lower than the population in general, the U.S. population in general and far lower than the relevant city rates; in other words it was just the opposite way. There were only two plants that showed any association and the relative risks for these plants were extremely low, they were like 1.2, 1.3. Adjusting for smoking even in the papers upon which the Board of Governors relied upon, which showed that one of these plants, all the association was associated with smoking, it had nothing to do with beryllium exposures. So six out of the seven plants showed nothing. The last plant adjusting for city rates instead of the U.S. rates also showed that there was no association. If you looked at all the data collectively, that is to say from all seven plants instead of cherry

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picking plants that would have also shown no association whatsoever. Despite this, beryllium's designation was changed from being a probable risk association with lung cancer to almost a certainty. I believe that this experience reveals that NTP's processes are severely deficient as are its criteria as applied in practice. NTP should revise its process and its practices in applying its criteria. Reconsideration of beryllium and beryllium compounds will be a good place for NTP to start in applying improved processes and procedures. Now the documentation for everything that I've told you was contained in the footnotes to my, to my comments, so if you have any detailed questions you could refer to those. Those are my comments.

DR. GOLDMAN: Thank you very much. Questions? Yes.

DR. ALLABEN: Looking at, at your written comments, would you say that you have several problems with the review process, they're all specific toward beryllium. Would you say that these were

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endemic to the entire process, or that beryllium just got a short shrift here?
DR. ROTH: I would, well, the fact that there were... I, I only attended the beryllium hearings, okay, so I couldn't tell you about the others. But I saw with the short time period they were covering nine pollutants in a very short period of time, and for the other chemicals I know that there weren't any, there, there was maybe one epidemiologist and I'm sure that with the other chemicals epidemiology was also of concern, so even though I didn't attend the other sessions I would assume that it was also endemic to the other chemicals as well.
DR. GOLDMAN: Can I just ask a question just for clarification? I'm thinking back, I'm trying to remember, which Report on Carcinogens contained this listing change?
DR. ROTH: Is it the 10th report?
DR. GOLDMAN: It was in the 10th,so it was the last...

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DR. ROTH: Right.
DR. GOLDMAN: ... the last one and as...and I know that you commented the last meeting so you've obviously observed some of the changes that have occurred in the process and I was wondering compared to then and versus now where you see the changes having been made and more broadly what you think are the most important areas that need to be addressed. Because, I mean some of these things like bringing in more experts, they have made that as a change, I think there probably would be more epidemiologists today and so forth, but maybe some of these there haven't and...
DR. ROTH: Right. Well, again, are you talking about process or are you...
DR. GOLDMAN: The process, yes...
DR. ROTH: Okay.
DR. GOLDMAN: ...in terms of the subject matter of our meeting...
DR. ROTH: Right.
DR. GOLDMAN: ... today, I'm

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trying to get back to that and, and...
DR. ROTH: Right.
DR. GOLDMAN: ...what, in the bigger picture just looking back from that, your experience obviously with the compound, but what you've learned from that and what you would like to communicate to us about what you think needs to change.
DR. ROTH: Right, I have a great deal of difficulty just in doing my job and working with the technical portion of things, process is generally way beyond me, but it seems to me that there are things that you could do, number 1, if you don't have an adequate number of epidemiologists on staff, which is, and the issue is epidemiology, then you shouldn't approve anything until you know you have an adequate number of epidemiologists on staff, and the other things are pretty well laid out. For example, there maybe should be very, there should be specifics up until what point do you accept published papers, like here our paper was published in the peer reviewed scientific literature two months in advance

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before the document came out and it seems to me that you should try to take advantage of all this latest information. And you know, the other things that I addressed I think it's fairly obvious what the next step should be, you know, if, there should be an opportunity for commenters to hear the criticisms of their work, or you know, where it's accepted and not accepted. So the process should make sense.
DR. GOLDMAN: And your paper, is that the Levy and Roth 2002, is that the one...
DR. ROTH: Right...
DR. GOLDMAN: ...that you're referring to?
DR. ROTH: ...right, and it's published in Inhalation Toxicology.
DR. GOLDMAN: In Inhalation Toxicology. Okay, thanks. Any other questions or comments before we... oh wait.. go ahead....you first and then.
DR. MOURE-ERASO: I would like to first make the comment that I, I, I am amazed of the lengths that you have gone

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to continue trying to save the good name of beryllium through the years. I have been following your presentations and it seems that has been a tremendous effort that has been put. One question that I have on the specifics that you recommend is you, you are saying that if a reviewer on the Board of Scientific Counselors has been involved in producing a scientific study that somehow relate to the issue that that person shouldn't be allowed to, to be a reviewer?

DR. ROTH: That, that individual was pretty much an advocate that beryllium is a carcinogen, you know, he had an axe to grind before he came and they didn't even pay attention to our paper whatsoever.

DR. MOURE-ERASO: Yeah. I, I disagree with you very, very strongly. I don't, I think that we aren't talking about having axes to grind, probably there would be other persons here that have axes to grind, I, I, I disagree with your characterization of the person that you pointed out here.

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DR. ROTH: Right. At a minimum the individual should have looked at the latest scientific research which was a published paper and not only was it just a general scientific paper, but the issues that were discussed at the meeting was whether or not there were other confounders that could have explained the elevated levels of beryllium lung cancer. And the issues were smoking, whether or not...what rate should be used as a referent population and whether or not all seven plants should be considered as opposed to one or two plants, these were...

DR. MOURE-ERASO: Yeah, I, I heard, I heard...

DR. ROTH: These were the precise...so the paper was extremely relevant, it addressed...

DR. MOURE ERASO: But you know, the objective of, of our exercise here is to discuss how could, how could we improve the process, I don't think that we want to re-litigate all the aspects that you have repeated over and over in every forum or the beryllium industry has, I think... I

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think that is not useful.... if you can make some recommendations specifically some procedures that would be helpful...

DR. ROTH: Right.

DR. MOURE-ERASO: ...but you know, I don't think...I don't think that you are going to have a second bite at the apple...

DR. ROTH: Right.

DR. MOURE-ERASO: ...to try to declassify beryllium...

DR. ROTH: Right.

DR. MOURE-ERASO: ... in this forum.

DR. ROTH: Right, well, I think at a minimum, at a minimum they should be reading and paying attention to and giving credibility to the published papers in the open scientific literature.

DR. GOLDMAN: Point well taken, and, and I think your point about mak...you know, having a clear idea of a cut off for when papers will not, can no longer be brought into the process is an excellent point obviously, logically.

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DR. ROTH: Mm-hmm. (Indicating affirmatively.)

DR. GOLDMAN: Every day there's a new paper and you have to have some way to stop the flow in so that you can analyze what's there and that just needs to be clear. I thought that was a good point. Let's now move on. Amy, I'm...we have to...you know, we only...oh, Bill had his hand up, I'm so sorry, Bill, it's hard, my eyes in the back of my head are covered by my hair.

MR. KELLY: I'm sorry, I'll try to be very brief. This again goes back to the issue of making sure that the nomination is correctly described from the outset. What, it, perhaps my recollection is faulty, but wasn't there with beryllium an issue of worker exposure coincidentally to Sulfuric Acid mist and did not, did that have a bearing on the carcinogenicity issue?

DR. ROTH: Right, that, that was another issue that I didn't raise but the one plant that had the highest levels, relative risk of about 1.4 the.. that used

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Sulfuric Acid and it was listed the, there are individuals that thought that that could be the association, that could be the, the confounding factor, that could be another confounding factor, so you're right, Sulfuric Acid was another issue.

DR. GOLDMAN: But that sounds to me like an issue for the epidemiology review in terms of if there's confounding...

DR. ROTH: You're right.

DR. GOLDMAN: ...and not in, and not so much an issue of the nomination to me but...

DR. ROTH: Right, but it's, it's a technical issue.

DR. GOLDMAN: It's a technical issue. Why don't we go ahead now, I'm seeing here the numbers of speakers that are left are dwindling down and we've got two more on the list. Are there others that I'm not aware of who are here to speak because when I just again kind of, it's noon and I said we'd break for lunch now, but I'm tempted to say we could move forward with the last two presentations and then break

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for the day. Now if people would find that to be an appealing alternative, I don't think that the lunch options around here are necessarily the greatest, but I want to check in also with our last two presenters and, and if any of you were counting on the lunch as well for some reason, you don't have to say what it was... Amy, what, what's your pleasure?

SPEAKER: I think we should go ahead and...

DR. GOLDMAN: Go ahead?

SPEAKER: Yes.

DR. GOLDMAN : Let's forge forward then and let Ann, you want to, you want to have a...let's give people a 10 minute break, 10, 15 minute break. Chris?

DR. PORTIER: I would feel a lot more comfortable if we came back after lunch and just summed up and continued. I don't want to feel like we are rushing through these public comments. There is no reason for rush, we can do your comments before lunch. There's good reasons to do them before lunch 'cause many may not come

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I want to make sure that....

DR. GOLDMAN: Because I'm afraid that we will lose our audience.

DR. PORTIER: I, I want to make sure we, it's clear we have plenty of time, we'd like to come back after lunch in case there are people who show up. I, I don't want to rush this at all.

DR. GOLDMAN: Do you want to go ahead and give your comments now and then perhaps we can have both comments before lunch, take our break, come back and make sure that we've discussed and summarized.

DR. PORTIER: And I would appreciate a five minute break right now, yes.

DR. GOLDMAN: Well, Chris, if we're going to take a break now since it's noon why don't we just break for lunch then? I mean, it's... that's my sense, is that okay? Yeah, why don't we just take a lunch break and what time do you want to come back?

SPEAKER: You're the Chair.

DR. GOLDMAN: Say at, how

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long does it take to get lunch here?

DR. WOLFE: The, the lunch options are basically to go across the street to the Natcher building, there are just, there's very limited food downstairs because they're renovating the cafeteria. But right across the street in the Natcher they have like a full surface cafeteria with sandwiches and salad and some hot things, so it's just right across the street.

DR. GOLDMAN: So why don't we say that we'll be back here by say 1 o'clock? That's a bit of a walk, and people have to bundle up to go back and forth so I apologize to you, Ann.

MS. LE HURAY: If I could just do one thing before lunch, I'd like to answer Dr. Toraason's question that you asked about the, Dr. Roth about beryllium, because if we look at NTP's comments in 1999 at a similar meeting I think we had something like 9 or 10 one pages from different chemicals or substance groups describing their experience with the, with the process... the Report on Carcinogens process.

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And then of course we had Dr. Roth on beryllium and then Dr. Piccirillo will be giving an example from the 11th Report on Carcinogens, you know, to answer any issues you, people had, and that kind of, Dr. Roth doesn't have an overview of all the different people that had been inolved. Thank you.
(WHEREUPON, a lunch recess was taken.)
DR. GOLDMAN: Okay, I can't think of anything I really wanted to do. All right, we have a couple more presentations from members of the public and starting with the American Chemistry Council. This time I will, I'll actually let you go.
MS. LE HURAY: Sorry?
DR. GOLDMAN: This time I'll actually let you go.
MS. LE HURAY: All right, so everybody has to pretend that I'm Rick Becker, and like I said, through the miracle of modern technology Rick was able to e-mail me his slides. We also have written comments that are also not here today, but I've been assured by NTP that they will be made part

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of the record and up on the website and that kind of availability. But if anybody wants to see a copy of our comments you can certainly get in touch with Rick or myself or anybody at the NTP and we will be happy to give you comments, they might even be posted on our public website, I'm not sure about that. So essentially, the ACC comments, American Chemistry Counsel subcommittee, the bulk of the chemical industry in the United States has... would like to recommend several improvements to the process and to the criteria used in the Report on Carcinogens, and one way of strengthening the scientific quality is through strengthening the process. I believe that that should be obvious. The second is enhancing the public participation processes in the development of the Report on Carcinogens listing, and thirdly, we have some recommendations on the clarification of what the criteria should be for listing and de-listing chemicals as Carcinogens.
I'm just going to go ahead, go on and do a sidebar to say that in the discussion this morning we've been talking

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about listing, listing, listing, but of course if you look at NTP's website it's always listing/de-listing and there have been several cases of substances that have been de-listed and I think that the processes that are thought of should include talks about how do we de-list when it's appropriate. So I apologize for having to pull these apart. On scientific quality just to, to look at the...by the way, copies of these slides are available on the table outside and I appreciate greatly the staff here helping me to get the Internet downloaded to make the copies. But the found..., the foundation of the Report on Carcinogens listings and de-listing should always be based on quality of science. You know, as I had said in one of the comments that I made, the chemical industry is a science based industry and we employ scientists, we consult with scientists and we have a strong...have a foundational philosophy that regulations and any kind of decisions that affect our industry should be based on science. And we're more than

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willing at the, and I think that's been shown through time, if the science is...so indicates, to take appropriate actions even if it, you know, impacts on our industry and I think that that's been shown most recently in the whole P-Tox developments where 3M voluntarily suggested removing them from the marketplace. So anyhow, because the basis of the RoC should be quality of science. It should constitute comprehensive and thorough reviews and interpretations of the best available science. It should, scientific experts, those with specific knowledge of the issues involved should be involved in the process. The process, whatever parts of the process should be conducted in a manner that fosters a dialogue, and the decision making should be transparent and that goes hand in hand of course with the concept of fostering the dialogue. It means having open meetings, stakeholder involvement, meaningful opportunities for input and for scientific interaction. Any changes then to the Report on Carcinogens that NTP contemplates should be focused on ensuring that these changes,

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opportunities for input are enhanced. And of course, I mentioned earlier too in one of my comments that we have two new, relatively new directives that need to be thought about in the entire change process and that is what impact does data quality have to have on whatever goes on in the Report on Carcinogens and secondly, you know, how, how does the peer review requirements recently to come out promulgated by the Office of Management and Budget, how is that incorporated in this process?

Just to go on a little bit, but really I would like to see enhanced processes that include the public and stakeholder participation, enhanced opportunities and not just writing comments that for all appearances go into the void and we don't ever know if there's been a response to the comments, but actually having it as more of an interactive process. That's what it's all about.

So how do we propose to do that? We, at ACC a number of people were called together and we looked at the process as it

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was before 1999. When we looked at the enhancements to the process that were made as a result of the meeting held five years ago, when we looked at the further enhancements that you had proposed in the Federal Register Notice and we thought, our basic problem is not going to be fixed; in our view, the basic problem was the, was the process which supported this dialogue. By just nibbling around the edges, and we would urge NTP to think about doing a sweeping change to the current Report on Carcinogens listing process, and we would promote as a model for that change something that NTP has done and has done very well, that is science based, that allows the opportunity for scientists who know the substances that they're considering very well to be involved from the very beginning in what has been a very open and transparent process and that is something like we know it's not an exact duplicate, there would have to be some modification, but something like NTP, CERHR, that's the Center for Evaluation of Risk to Human Reproduction, which essentially

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evaluates the same chemicals to...for their reproductive and...for their reproductive and...

DR. GOLDMAN: Developmental.

MS. LE HURAY:

...developmental, thank you, for toxicity, and looks at that in specific. So that process has been much more open and that is part of our recommendation. In our written comments we get into a detailed proposal, not necessarily the final thing, but a detailed proposal of how the CERHR process as it currently exists might be adapted to the Report on Carcinogens process. Just for those who might not be aware, off of NTP's website there is a flow chart for the CERHR process, which shows right from the very beginning an open nomination process, anybody can nominate for listing, and in the case of RoC for de-listing. The nominations are reviewed by NTP who brings some of them forward, this recommended, recommendations, lots of opportunities in the beginning for NTP to consider all the various important aspects about whether there's data available,

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whether it's timely, whatever it is that needs to be done to take the process forward, but there's public comment very early on, and including the ability to nominate who serves on these, what they call in the CERHR process the expert panels. Now as I understand the process the expert panel, as Dr. Roth was mentioning earlier, would not include somebody who has necessarily a direct stake because of their own research or because they were involved in legislating a particular, or writing regulation for a particular chemical or they were directly involved as you know industry, people whose portfolio included that chemical, but they need to have the right area of expertise and the right set of expertise to consider the data for that particular chemical or set of chemicals, and as a result of being involved in the nomination process and also, now perhaps it's been different at other CERHR meetings although I don't think it's been vastly different, because certainly those of us who have been involved and talked amongst

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who've had what they might consider unfavorable outcome as well as those of us who've had experience with favorable outcomes agree that the process is essentially a fair process, that you can go in and talk and present your point of view and at the end of the day reach some sort of strong, scientifically acceptable and valid conclusion. So we told you what the CERHR was. Our written comments, the ACC's written comments, this is kind of a flow chart that we made thinking about how to change the RoC, adapt from the CERHR processes into the RoC, we're not sure of all of the legislative requirements for the involvement of say the executive committee and all the different government agencies, you know, so around the edges and those kind of requirements we may not have considered everything. But we tried to incorporate some of the regulatory requirements as we understand them that are incumbent on the RoC to include such as the interagency involvement with being a more open and interactive, transparent process, so in our

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figure and we also have some detailed writing about it. And then finally getting on to the second point, and I only have one slide about ACC's recommendation for the criteria for listing and de-listing and we could certainly say a number of things about the criteria used by IARC or by EPA, but just focusing on the criteria that NTP uses, we feel like there's the distinction between known human carcinogen and reasonably anticipated has been blurred to the point where the public can't really distinguish the differences. And so we would suggest some changes that we've discussed in more detail in our written comments that would clarify the distinction between known human carcinogen, which would of course involve as well epidemiological evidence that, of in fact human carcinogenicity and making a distinction between that and reasonably anticipated. And then we also would agree with some of the other commenters previously today that the mechanistic information should be included as a guide to your listing and delisting criteria, so thank you very much.

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Rick did, but I'll try to answer any questions that you have of me.

DR. GOLDMAN: This was very quick, thank you very much. I do want to ask you a question, at the beginning you listed a number of points some of which you didn't go into in as much detail and I think, and there might be some shorthand here, but I want to make sure I understand them. Your slide that said scientific quality, the third bullet point you mention that NTP's efforts to revise the RoC process will be advanced by activities to address data quality and peer review directives of OMB. I don't know if you can expand on that, either here or, you know, when... perhaps it's expanded on in the written testimony, but I would just like to understand what is meant by that?

MS. LE HURAY: Well, it's ACC's belief and, that NTP's activities and, and work product, shall we say, such as Report on Carcinogens, the background document for the Report on Carcinogens as well as other materials like the CERHR

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monographs and the technical reports, the ACC, maybe not the technical reports, I'd have to look at that, believe that these are subject to the Data Quality Act and therefore it's incumbent on NTP in the process to ensure for the three principles in the Data Quality Act which are utility, transparency and quality and there's specific definitions in the DQA of what each of those items entail, but for example, to take an example of utility, if you are talking about chemical A and you use information about chemical B to make a decision about chemical A, you have to show why that is useful, that information about chemical B is useful in reaching a decision about chemical A. And they have...so, so then on peer review tho..., those, those people in the room who have dealt with the American Chemistry Council know that we strongly believe and promote peer review as a way to ensure that the best quality science is produced by any kind of process, whether it be published in a peer reviewed journal or published by government agency or science that we in fact

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through the long range research initiative. There's a strong peer review element in that.

DR. GOLDMAN: Are OMB's peer review directives in draft or final at this stage? Are OMB's peer review directives draft or final comments to this audience or is this more a comment that you're making to OMB?

MS. LE HURAY: Well, I think it, I think it's a two part, okay, because I think that while the draft peer review, you're correct that they are currently drafts, however, and I am not an expert on either of these, I'm just giving you my understanding of them, and my understanding is that it does apply to the executive branch and that OMB did issue a directive to the executive branch that the peer review directive was to be adopted. Now I could be mistaken about that, but...

MS. BECK: I can clarify that. This is Nancy Beck from OMB. We released a draft bulletin on peer review and we've received lots of comments from the

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process of going through those comments before there'll be any final bulletin, so right now it's just a draft.

MS. LE HURAY: Well, thank you very much because I wasn't sure, but in any case, we, you know, eventually presumably there will be a peer review requirement and, and it's better to think about how to incorporate that now than to wait until after it's implemented and then have to go back and make changes.

DR. GOLDMAN: So then, one last question then, so the proposed outline of a process that you presented in your last slide, is that to address all of these points or...?

MS. LE HURAY: Well, it, it, I would have to look at the, at the written comments, but I know that in the discussions that we had, my understanding of the process that was proposed, it was proposed that the, what the equivalent in the CERH process was called the expert panel review, that that would qualify as a peer review step as in, you know, and fit within the peer review

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criteria as we understand it being developed so, so I don't think that there's anything additional proposed to, to meet it.

DR. GOLDMAN: Dr. Portier has a question and then I'll ..... there are some other questions up here.

DR. PORTIER: Yeah, there was one additional step in your proposal for the modification of SEER and I did want to ask a little bit about that.

MS. LE HURAY: Okay.

DR. PORTIER: In the SEER process the expert panel report is submitted for public comment and given the public comments on the SEER panel report and the report itself, the NTP does a final monograph, which is not sent out for public comment or peer review prior to the release of our public monograph, whereas here you have in the RoC process, I believe you put that in there. NTP draft monograph.

MS. LE HURAY: Right, and that, that's one of the exclusive changes that we would recommend go through the CERHR, as a matter of fact, that lies within

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there, as well as for the RoC. That there be a draft and final monograph, to allow an additional opportunity to comment because, you know, we just love writing comments.

DR. PORTIER: We appreciate the comments actually. Again, it's something we will consider and, and look at very carefully, it's a, it's an interesting proposal. There are some slight differences between the SEER process and the RoC process in that the SEER process is an NTP initiative, it's our choice to do this, it's something we thought was important as a public health initiative as compared to the RoC which is a statut..., statutory requirement that the Secretary has assigned to us, so it's a slightly different process in that the Secretary makes the final decision, not us in the RoC. Just to note that slight technical difference.

DR. GOLDMAN: I think if you could...oh go ahead.

MS. LE HURAY: That's all right. I was just going to say I think we appreciate that although we didn't understand

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all the implications of that, but, you know, I mean the good news from our perspective was that, you know, industry overall has had a positive reaction to the CERHR process and while we were trying to, you know, see, well, what additional changes were, you know, what was the effect of these changes that you proposed in your Federal Register Notice, what would be the effects of all these? Well, this answers a lot of what industry's problems have been historically with the Report on Carcinogens, because even implementing some of the changes that are suggested in the, in the Federal Register Notice, I think that everybody recognizes that industry's basic problem is I, things that I had mentioned a little earlier is that we're a science based industry, we deal with science and we would like to be able to talk about the science and not have it so... and not, not have our interaction be relegated to the regulatory stage. Dr. Goldstein's comments were I thought very good, but I think that he needed to, to, to refine it perhaps to understanding that our

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the, the data that are out there and the processes that our chemicals, the health effects of our chemicals, than anybody else does, and, and we just think our input is very valuable and it's very frustrating when it doesn't appear as though anybody's listening, so.

DR. GOLDMAN: Well, that's what we're here to do now. I think a number of questions from the panel, and I'm going to go ahead and start with Dr. Carpenter and just work my way across if that's okay and you probably want to leave that up.

MS. LE HURAY: And if I may just state, remember again, I'm not Rick Becker so...

DR. GOLDMAN: We know.

MS. LE HURAY: And I don't even plan on being.

DR. CARPENTER: So what the American Chemistry Council is suggesting is that the, the Board of Scientific Counselors would be removed from this process?

MS. LE HURAY: Quite frankly, I mean the CERHR does not have a Board of

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Scientific Counselors step, at least not one that I'm familiar with and so we would suggest that they would be replaced by this expert panel. Now perhaps...

DR. CARPENTER: Which would be chemical specific, each, each...

MS. LE HURAY: They would be chemical specific. Well, I think in our written comments, if I'm remembering correctly, that what we suggest is that perhaps there could be like a core group of some sort of core committee that, that could be like a Board of Scientific Counselors committee, but that you would explicitly bring in some additional people who are explicitly have expertise in the issues that are important to that particular chemical or set of chemicals. Now in the CERHR process it has, I think we've been through about, what, five or six cycles since the process was re-instituted at the CERHR and there's been one Board who've covered a number of related chemicals, so there's one that was just about a year ago, February of last year, only covered two, but they were two

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light bulbs, so it was definitely light bulb, propane light bulb. And then there was another one that did four or five or maybe even six studies altogether so now, but I don't think that there is a BSC subcommittee involved, am I wrong about that, in the CERHR process?

DR. PORTIER: The Board of Scientific Counselors reviews everything we do with CERHR like all other aspects of the program, but there's no specific subcommittee for CERHR.

DR. DELZELL: Is, is there...I know the, the CERHR process is, CERHR process is relatively new, but has there been any aspect of it that you would criticize?

MS. LE HURAY: I know that there have been... at one point, though we think that that issue was resolved there was some conflict of interest questions about who was named or nominated to serve and I think that those have been resolved, but quite frankly, the, our biggest fear about going in this direction that I'm suggesting,

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proposing that NTP consider going in this direction is that we are aware that the current process could be... has been greatly influenced by the participation of, of Jack Moore and his, you know, perhaps unique ability to be inclusive and to understand who to include and how to get this done and how to, to run it properly, but we think that that's now been institutionalized, it's been through, like I said, through four or five cycles and our hope is that it won't become a process where it all relies on one person. So the process has worked very well up 'til now, and we think that it's not just Jack Moore's involvement that has resulted in, in a very open and inclusive process.

DR. GOLDMAN: Okay, I can tell you as I've, I've looked at the process quite a bit over the years and the two issues that have been raised again and again have been the extent of the effort and commitment by the outside expert panel members, it's a tremendous amount of effort, and many people after doing one have sworn they would never do another, because it's

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been nearly their entire job, you know, for a couple of months to do it and nobody's of course hiring them to do it. So, it's a lot to ask volunteers to do and the second thing has been the pace and the productivity. If you compare the outputs with the outputs from the RoC it's really no comparison at all, it's a couple of orders of magnitude different, so figuring out how to make that kind of a process work that fast and then, you know, maybe part of why people have liked it is because it has been slow so there's been a lot of time taken, but then you don't have the public health benefit of the analysis having been completed at the end, so...

MS. LE HURAY: If I may just add to that, I mean, another process that, that, that is, has, has, is more like NTP than CERHR, but that it has been more inclusive in many ways, has been the IARC process, and that's very different than what NTP, you know, have done in this process, but like Dr. Goldman was saying, they take a smaller number of compounds to review at any

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one time, it takes a long time, you're right, I'm sure that the people who are manning and woman-ing these expert review panels spend a very large amount of time on, you know, the work product has so far been quite extensive, and they take ownership of these expert review reports. So, you know, since they're taking ownership, their name is on it and that means they're going to spend a lot more time on it. But we think that in the end the result is a lot more acceptable to, to the regulated community and perhaps you would find that it wouldn't have actually taken more time. I don't know. You'll have more experience than you need, I think, for that.

DR. DELZELL: The other thing I, I wanted to ask you to comment on if you'd like to, is that you and several other people have mentioned that the, the peer review response to public comments is often not satisfactory and do, do you have any comments about mechanisms for doing that?

MS. LE HURAY: Well, this is the difficulty of my wearing the ACC hat

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the, in, in that regard. How to and, and I think that part of the overall problem, the more standard problem, in my narrower personal experience has been that the, the peer reviewers, as I think Dr. Roth had mentioned, are reviewing anything from, you know, 10 to 12, perhaps a few more, few less at any given RoC subcommittee meeting. They have maybe an hour and a half to two hours to spend on any given chemical, whether it's one with very complicated issues or one that there are no complicated issues, or at least no dissent from the complicated issues. I know I've been to RoC peer review meetings where there have been nobody to give public comments, and I, because I was somebody who sits in the audience, nobody in the audience who's really following what's going on with a certain chemical. But then there's other ones where there's been a number of commenters but I think the members of the, of the peer review committee, I don't know how it is that they operate, but I don't think they have a lot of time to review all the materials they've been given,

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including comments from the public, and I would venture to guess that perhaps one of their charges is not to specifically make sure they're familiar with and respond to those comments from the public, because none of the proceedings are ever made public, you know, other than the court reporters putting out a transcript, that's the extent of what is ever made public about those RoC meetings.

DR. GOLDMAN: And I can, I can tell you my, my impression having served not on the RoC subcommittee but certainly on the BSC, that it seemed to me that the members did feel that it was their job to not only read all of the background document but also all the comments that had been, that had been submitted in. I think most people do do the work, you know, do the homework, but I can really hear the frustration that you feel of seeing the issues go by quickly without really seeing a lot of discussion and I mean obviously that, that would be frustrating and I think that that's something that we've heard earlier

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today as well, so it's a, it's an important point. You wanna, Chris?

DR. PORTIER: I, I want to echo some of Lynn's points about that, that, those being very important points, I just want to make sure I didn't hear something incorrectly. The RoC meetings, the, the public part of the RoC meetings is the whole meeting for the Board of Scientific Counselors. There are no additional meetings of that Board that occur other than in that public meeting. The laws of the FACA require that. I will note there is a substantial difference between the IARC process and the RoC in that none of the IARC meetings are public. The votes are not public, what's included or excluded from their documents is not public, it's a very closed process, so, and, and I think you want to be very careful in making that comparison given some of your other comments about openness.

MS. LE HURAY: And I, and I, and I agree, and I should have left them alone, you're correct, because it's not something that ACC is proposing, that, that

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NTP add that language, so thank you.

DR. GOLDMAN: I want to keep, I want to keep moving down the table and then there are some hands up in the audience as well but, no. Mark?

DR. TORAASON: Two questions. One is, on this particular slide, one thing that I'm trying to incorporate here is a hallmark of the RoC and that's this voting process that, you know, RG1, RG2, RG3 and you sort of have a tally, which I think probably plays heavily on the director in trying to make a decision seeing how these group, and I don't see that in here, or having a real clear idea of how you would either just get rid of that or incorporate it into this. The other question is, the NTP has a mandate to, to list or not to list, do you think what you're proposing is actually going to have an impact, I mean there are, are there examples where the outcome would actually be different if you added all this extra elements of review or are we adding more, something more to achieve the same end?

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MS. LE HURAY: I, I, I would say, to respond to your second question first, I would say that it could impact potentially outcome in that if you include in outcome what is the documentation for the decision that's made. The documentation for the decisions that are made now, as you all know, the RG1, you get a short summary without any discussion of the basis for the vote. For RG2 you get a short summary without any discussion of the basis for the vote. For the Board of Scientific Counselors, you get a summary and it's, and you don't get a, any kind of a sense of the often quite intense discussions that happen in those one and a half to two hours that you have to devote to, to your chemicals. So to compare this with the RoC process, what we're really doing when you think about it is that up through the point of the final expert panel, a lot of what we're doing here is proposing a new way for developing the background document. Okay? And it's much more focused on, you know, involving the experts, involving industry, talk, talking at

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the science level. Now we go then it gets turned into what we call here a monograph because we're simply duplicating language that the CERHR is using, which as they call there the NTP produced document, a decision document, if you will, the monograph, and so how, how that exactly would be, how, how it would work to fit in, there's some sort of a requirement that we have in RG1 and RG2, you have to duplicate those, but then I think that could be worked in, but it would happen after the final expert report was issued, I think is where it, would be where it would fit, and so it might be beneficial, though, to these groups to the extent that the expert panel would come to some recommendation.

DR. GOLDMAN: I mean, in essence, you're also in a sense eliminating the background document step in that the expert panel is writing the document, the... in a way that the draft expert panel report might be the background document although it, it has seemed to me, I've observed a couple of the CERHR efforts that, the CERHR staff

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do put some effort into filling the information, you know, at least the scientific data, you know, in, in a, in a way they have it, and in some sense they do have a background document but it, it isn't called that and it gets worked over by the expert panel before it becomes a draft and so ... you know, I think that's another thing that's worth thinking, someone has to do that work, right, for the reviewers?

MS. LE HURAY: And I'm not sure, you know, what happens behind the doors of the CERHR, if you will. I mean, the expert panel puts their name on this report, the initial draft which is the peer review draft, who prepares that, what sort of process it goes through, that's very opaque to me. I mean I have seen some of those peer review jobs and seeing that there's, you know, uneven quality, some are, are more complete, some sections are more complete than other sections, but that's to be expected, you know, in something that's a draft, but how that's produced I'm not certain. And I think what I, what, what ACC

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is, is suggesting is that the overall amount of interaction and transparency, that, you know, nothing is ever going to be perfectly transparent in this kind of a process, but that certainly there could be a lot more dialogue earlier on in the process, and I think it would behoove everybody and improve the process from everybody's perspective.

DR. GOLDMAN: Question from the audience, please identify yourself?

MR. NIDEL: I have different kinds of reactions maybe to what you just were talking about. The first is regarding the scientific quality, it seems like maybe the posit..., you know, it just seems like there's an aim to focus a hundred percent on science rather than any bit on policy and I guess from maybe an uneducated public perspective it seems like we have to remember that there is a policy element to this despite the fact that the focus is on getting the science correct. You know, this, the Report on Carcinogens has very policy based impacts and I think that there are policy considerations that should be

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taken into account that are not going to meet the same strictures as a scientific standard. You know, an example would be the kind of evidence that the government would use to elevate a terror threat. If it's, if it's a threat of great magnitude they're not going to, you know, the credibility of the evidence may not be as great, which brings up kind of a conflict between the industry and the policy which is, the greater market there is for a product, the greater desire the industry has to hold it to scientific standard because this is a profitable product that's, you know, going out to many people. But from a policy perspective, that's even greater weight in favor of the precautionary principle and trying to protect the public from the impact of that compound, I think you brought up the 3M example and I, I may not have the full, I mean I've read various, you know, accounts of that example, but from what I understood it was based on, that they recalled based on the findings that Scotch Guard or these compounds were in the blood of people all throughout the globe rather

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than some scientific evidence that said that that was necessarily a health threat.

MS. LE HURAY: I, I do not know the details myself of the P-tox example, but let me respond to two questions that you asked. One, one is, I mean, I, I don't think that from a policy perspective that this proposal makes any changes to what I think I've heard most people say here which is that policy discussions come after the NTP has reached their conclusion. This would still keep that conclusion, you know, based on science, leave it up to the, the regulators or policy makers to take that conclusion, that whatever it is that NTP reaches, and apply what they think is appropriate to do with it. So, for example, to, to stick to the CERHR example, California also uses the CERHR as an authoritative body to identify compounds as developmental or reproductive toxins and they have regulations based on that so, so NTP reaches the scientific conclusion. This is whatever, low concern, high concern from the point of view of develop, developmental or

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the state of California goes forth and regulates on that basis. So the policy, I, and I think that's what I've heard before. Then the second thing that I'd just like to say is that in fact it's just the other way around typically, which is that typically your lower volume chemicals are more profitable than the commodity chemicals that are out to, out there, you know, used in great bulk, because typically lots of those are made and the prices are very low.

MR. NIDEL: Well, I, I think, I mean, that probably depends a lot on the product. My, my other response to what you've said is you, you've referred to industry as being scientific and knowing, you know, kind of in a, just having, having a good knowledge of these compounds and of their chemical, you know, properties and potentially their, their health effects and I guess what strikes me as someone who is a scientist that used to work in the industry, I don't necessarily agree that that's true and I just want to say that to take, I guess my comment is to take what you're

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with some caution because I mean I've worked with chemicals that had come out that were listed in the 10th and the 9th report that were never indicated to me by the industry that I worked within and for, to be of any hazard. So I think that there is, there is, it's, it's not a hundred percent that the industry knows best, I guess is what I would say, even though they may be the people who, you know, have patented or invented or you know, come up with and handled these compounds in huge volume.

MS. LE HURAY: Well, then, I think we have a basic disagreement, but I think what we can agree on is this, that to the extent that science is never going to be a hundred percent knowable because it's science, it's not engineering where you can have an equation and fill in the slot. Industry has gone to great lengths to learn about these chemicals and usually, maybe there's exceptions, but usually industry will try to know a little more and does know a little more than people who have not focused on those chemicals because they're not

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focused on learning about those chemicals, and that's one thing we do, I mean, we try to know our products, so.

DR. GOLDMAN: Anybody else? Okay. I guess one more, one more question.

DR. MOURE ERASO: It seems that, that your proposal what I notice is that you basically have very little confidence on the expertise or scientific ability of the people that do the work in the NTP and NIEHS and the animal experiments or the people that are called to be in the Board of Scientific Counselors?

MS. LE HURAY: No, we, we think that's not the case at all and I, I would be the last person to, to personally and I think that the ACC as well, to, to question the credentials of any of the people because we know the good work and we are as supportive of much of the work that NTP does as we sometimes will be critical of the work that NTP does. It all depends on circumstances. But we think that everybody's in a bad situation and particularly the Board of Scientific Counselors because quite

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often we will see, you know, you've heard other people say, for example, with the background document which is, you know, the basic document on which it's supposed to be, which is the document of record supposed to present the, the data on which decisions are made. Sometimes that's not available until very late in the process. Now I know there's been a concerted effort to try to make that available earlier and that's one of the proposed changes that Dr. Jameson has proposed in the Federal Register Notice to the RoC process. But it's still been the case in the past and we would hope that it would not be in the future, if the process were not to change, that, I, I have spoken with people who served on these boards and one thing that I have taken away from it is that they feel very inundated because oftentimes very late in the process, sometimes a week or two, and if they're lucky three or four, before the actual meeting, mounds of paperwork all of a sudden start appearing in their office. Which includes the background document, the public

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comments. You know, if you have a longer period of time and you're reviewing, say, ten chemicals but sometimes the, the timing is very tenuous, and we've experienced that because we oftentimes want to present comments and we have perhaps one chemical to review and feel as though we're being stretched for time. Now perhaps it's, it's different.

DR. MOURE-ERASO: But your, your proposal is pretty radical... you're saying, you're saying to basically dissolve the Board of Scientific Counselors and stop NIEHS to prepare the draft document and give it to a panel of experts that supposedly will, will come from another side, and it's pretty radical.

MS. LE HURAY: Well, and I agree with that, but I also think the Board of Scientific Counselors to be able to look at this would not be involved in developing the background documents in any case.

DR. MOURE-ERASO: Not supposed to.

MS. LE HURAY: Exactly.

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DR. MOURE-ERASO: They're not supposed to, yeah.

DR. GOLDMAN: And I think, I think that it has in common in both instances in reality there's a background document that is developed by a contractor. Maybe in one case it's more visibly that than the other but the I.... as far as I could always tell in with the process for the developmental and reproductive toxicants that the contractor does get it started. Even though the expert panel finishes it, there is that support that's given to the experts. But I, I would agree that it, it would be a very radical change, it's a...

MS. LE HURAY: And, and that's, that's one of the things that we recognize right at the very beginning, that this is a sweeping change that we're proposing, but we would suggest that we, we had changes that we proposed at the meeting five years ago, and there were, some of those changes were implemented and incorporated, but some of our experiences in the last five years have been not that much

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different than the experiences were before some of those changes were incorporated and we said okay, well, why is this, what is at the heart of the issues that we have? And it really has to do with having a chance for real input by the public early in the process. Currently the, the opportunities to comment come very late in the process, after, essentially the science has been reviewed in the background document and that's the, the, you know, it's said to be the, the document of record and as Dr Portier said earlier, you know, once RG1 has, has reviewed it, there's no changes. Well, we do not, the public doesn't have a chance to comment before RG1 has reviewed it. So it, it, it's kind of a little loop system where, where we're frustrated by that lack of involvement.

DR. PORTIER: I'd like to make a correction. At least from my experience on the Board for the last four years, I'm finishing up the fourth year of my term, a week or two, that's clearly not the case. These, these background documents are, are

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Oftentimes the inundation of, of materials toward the end of the time period that you're looking at are public comments. Those are things that are being, coming in late to us and because we all do make every effort we can to look at the public comments, personally I guarantee you that that goes into my consideration of, of the information but that's what takes the time right at the end, it's not the background documents.

MS. LE HURAY: Yeah, but part of the reason for that is that the public comments, the background documents are not made available to the public. You're seeing it for the first time. Dr. Piccirillo, who's giving the last speech of the day will be talking about a case where the background document was made available, I don't know, was it six or seven weeks before the RoC meeting and because we were trying to, you know, get the comments in time for RG2, we put together those comments in 10 days. But you know, this is, we're not making comments on policy here, you're making comments on science and that sometimes take a long time

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to develop. So if I had a wrong impression, my, I think our impression is based on when things get posted on the website. So...I'm, I'm glad to hear that it's different for the RoC committee.

DR. GOLDMAN: That's good to have that clarified. That's important because, I mean I do think that there was a time several years ago when there, there were documents that came late and so maybe that's an impression that has been left but I hadn't heard that for a long time either. Okay, well, if it's okay with everyone, I'm looking around here, why don't we go ahead and move to our last speaker?

MS. LE HURAY: Well, I thank you all for your patience, because like I said, I'm not Rick Becker.

DR. GOLDMAN: You, you're better than Rick Becker. We, we were pleased to have you. Thank you so much. Yes, Chris.

DR. PORTIER: While we're moving to the next qu..presenter, I'm going to make a few comments about the SEER process to make sure it is clear since this

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is an opportunity for a public comment on it and we... it's been mentioned... I'll make a couple of public comments. First of all the SEER process is changing, we want to be certain that we are in fact in line with current peer review practices of the U.S. government. And so the panels that make up the SEER review committees are no longer going to be ad hoc NI..., NTP panels, they will in fact be special emphasis panels which is a special government type of issue and it's going to have, they will have a slightly different make up to them than they have previously, you will see because of that factor. There's a number of things that will be changing in that process you should be aware of, and I would just keep an eye on it since you've paid so much attention to it. I would keep an eye on it over the next few months as we actually change the way in which that process works, again keeping in line with what's happening within the U.S. Government.

DR. GOLDMAN: Could you, could you, what do you mean by special emphasis,

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just so... put it in English so that...

DR. PORTIER: It's hard to put into English. The...you, you can think of panels as falling into three different categories. So you are made up of, to some degree, representatives of our Board of Scientific Counselors and past and present and Executive Committee, past and present, but as such you're an ad hoc advisory panel for NIEHS in this particular capacity at this particular time. In those cases we can pretty much put whoever we want on such a panel. If we really want something to, to, to match up to where we, the, the Federal Government thinks should, thinks should be in terms of balance of expertise, balance of location across the country, gender, et cetera, then in fact we move into a more formal category and special emphasis panels fall into that category. It changes the way the members of the panel are viewed as to whether they're government employees or not government employees as compared to in this capacity, you are not government... you're not actually government employees, you're

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coming in as a one day advisor. In those cases it's a slightly different set of rules on conflict of interest. Then finally you have a third level of advisory panel, that's our Federal Advisory Committee Act fan, panels, those are formal panels, they're, they stay for long periods of time. Our Board of Scientific Counselors is such a panel. There's an actual process involved in getting names on to such a panel, in review of such a panel, there's formal evaluation of conflicts, number of issues go into that, so, the SEER panels are moving up out of sort of this ad hoc into the special emphasis panel category because we feel it's appropriate for the activities they do. The Board is a higher level panel in terms of the activities they do in the requirements for evaluation of their efficacy on that panel or whatever.

DR. GOLDMAN: So, basically what he's really telling us is that we're not special. Okay, there's another piece of testimony that has been brought in from James McGraw. It is several pages long and

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to spare all of you the agony of hearing me give it a dramatic reading, what I'm going to do is virtually read it into the record, kind of like the way members of Congress read things into the record. If you've ever gone to a, a congressional hearing and then you see the hearing record and later they're, it's there. If that's okay with everybody. We, we, we will pass out copies if everybody would please read the testimony, is, is that okay? Great. All right, so we have one last presentation and this is Vincent Piccirillo from Coppers and American Chemistry Council, the Naphthalene panel.

DR. PICCIRILLO: Good afternoon. The Naphthalene panel of the American Chemistry Council appreciates this opportunity to talk with you today and provide our comments on the review process used by the National Toxicology Program in the Report on Carcinogens process. I've heard a number of comments earlier today which actually paralleled the comments I was planning to make and so I will not spend a lot of time dwelling on those comments

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because you've heard them several times already. One of the main frustrations of the Naphthalene panel during the RoC process was the fact that it did not appear that there were really substantive opportunities for public input into the Naphthalene process. And I think that this comes down to the fact that even though it appeared that certain time lines were, were in place that for various reasons things were moving along very quickly, not allowing really the, the public input process to its full avail. As an example with the, with Naphthalene, NTP elicited recommendations on the listing of NTP through the RG1 process, the RG2 process and then took it to the BSC RoC subcommittee. Unfortunately the RG1 review occurred well in advance of the draft background document, the RG2 review then occurred before publication of the draft background document and we really had, and, and after and prior to the date of receipt for public comments. So we really were enmeshed in trying to provide comments, trying to meet these time lines and I think

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from some of the earlier discussions, if we had set time lines for the various reviews or the various time periods for getting in comments, this would really help the industry to provide substantive comments on each of these documents or to assure that the underlying science involved with the chemical does get to the hands of the scientific reviewers. We know full well that NTP spends a lot of energy in doing the literature searches and reviewing the literature they're able to find but if you look at the industry, they're spending a lot of time also looking at these chemicals and may be well aware of documents of publications which may illuminate the process of the, of carcinogenicity for a particular chemical.

In the current RoC process it really seems that it's the, the Board of Scientific Counselors subcommittee that is the principal opportunity for public engagement and it is based on this, these public comments that a lot of decisions appear to be moved forward. One of the things that we, we do feel is that the time for public participation should

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be much earlier than that in the process. As was indicated, the public actually has 7 minutes in which to put forward their comments on what could be some very complicated issues in regards to things such as mechanisms of carcinogenicity. Or specifi...specificat...specificities regarding the metabolism of the chemical. So it really doesn't give a lot of time to really get involved in the, the process with that, with that Board. With Naphthalene, however, there was something else that was brought up this morning which is very important to us. And this was the issue around the establishment of closing dates for submission of scientific literature or publications which would be relevant to the deliberations of the subcommittee. In the November 2002 RoC subcommittee meeting we sh..., we saw a case which we feel ne..., we need to bring forward to the group so that similar things don't happen in the future. In this deliberation it was obvious that the basic principles of the Data Quality Act, that is objectivity, transparency and utility, were

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compromised. And the rationale for saying this is because the subcommittee chairman temporarily stepped down from his job as the chair to join the discussion of Naphtha..., Naphthalene and to participate in the vote. The chair also then provided a document to the subcommittee members just prior to the break and suggested that the subcommittee members review that document during the break because he would be making substantive comments after the break. Following the break, the Naphthalene panel was given its seven minutes to make its comments and it was then followed by oral presentations by the chair, and this was a highly technical presentation to the sc..., to the subcommittee, including new information not previously shared with the subcommittee nor made part of the public record. The members of the public present at the meeting were neither permitted to see the materials on which these judgments were being based nor to ask questions or give additional information or clarifications to some of the things that were discussed. The ob...,

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objectivity, the transparency and the utility of the Data Quality Act process were violated for the following reasons. First, the work of several well regarded, independent academic researchers who've extensively published on the toxicology of Naphthalene and was presented in the draft background document were criticized. The widely accepted work was dismissed as being of little value by the chairman, who based on search of the literature, has not published any research on Naphthalene. Second, the public was not permitted to see either the newly submitted document or the publications that were said to form the basis of the documents at the subcommittee meeting. No public comment was sought either at the subcommittee meeting or since the presentation or were any changes made to the background document to reflect the discussions of the, of the chair on these new documents. Third, since the RoC subcommittee meeting, NTP has provided to the Naphthalene panel a list of three references. These three published papers were purported

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to be the basis of the document distributed to the subcommittee members at the meeting. The panel has reviewed this literature and found that these data are of little to no utility to the understanding of the Naphthalene carcinogenicity. In the absence of further information the panel can only conclude that the presentation made by the subcommittee chair was a personal opinion unsupported by published literature. The acceptance of the chair's privately distributed document by the RoC subcommittee without a review of these underlying publications calls into question the reliability of the decisions made by the RoC committee. We feel that it was important to bring these to your attention. It's very important that these reviews also be unbiased and we talked about bias this morning. We hope that these types of deviations will be considered in adopting some of the new processes for the RoC to hopefully avoid such situations in the future. Another thing that we feel is, is also very important is that the procedures for listing

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should be clarified. One of the things that came up during the subcommittee discussions was that one of the members was not sure how to deal with Naphthalene. He felt that it was essential to go back and take a look at other chemicals showing similar profiles as far as carcinogenicity in animals, genotoxicity, et cetera, to see how previous subcommittees had dealt with those issues. And it was his impression from going back and re-looking at the RoC, the 9th and10th RoCs, that none of the chemicals that had the same data or similar data to Naphthalene were listed. So we feel it might be important for NTP to try to put together some kind of a, of a guidance that would help in the committee's abilities to take a look at the data, see what kind of precedents may already have been set and then determine if this chemical truly does fit or not. This way, at least there will be some clear pattern for the subcommittee to move forward. Based on these experience, experiences, the Naphthalene panel fully supports the discussions that Dr. Le Huray

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made in regards to making some sweeping changes in the RoC process. Hopefully this will increase the transparency of the process and also lead to more meaningful science ba... meth..., science based methodologies. Thank you.

DR. GOLDMAN: Thank you very much. I actually want to start off with a question for you. I really can appreciate from your description of what happened at the, at the, I take it that was the BSC RoC subcommittee that you were describing...

DR. PICCIRILLO: Yes.

DR. GOLDMAN: ...that...I, I wasn't there so I can't really comment on it obviously, but it sounds like it would've been a fairly trying experience if it really went as you described it. I was wondering if it made a substantive impact though on the way things were going, I mean what, what were the votes like for the RG1 and RG2 committees and I mean did it, you know, did this like change the tide in the way things were going or, you know, where were things going before it went there?

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DR. PICCIRILLO: It, where it became very difficult, Dr. Portier would like, where it became very difficult for us is the fact that the RG1 vote was 6 to 1...

DR. GOLDMAN: Okay.

DR. PICCIRILLO: ...to list, the RG2 was 4 to 4.

DR. GOLDMAN: So RG1 was 6 to 1 to list, RG2 was a 4, 4 split.

DR. PICCIRILLO: 4, 4.

DR. GOLDMAN: Uh-huh. (Indicating affirmatively.)

DR. PICCIRILLO: Yeah, and...

DR. GOLDMAN: I mean...and I'm not usually focused on vote counting, I was just wondering how things were, you know, going before that.

DR. PICCIRILLO: What, what I felt was rather interesting is that there were some very good questions brought up by some subcommittee members which seemed to be, the decision was we can discuss these later, but yet when the discussion turned to these underlying documents some of those questions were really never answered.

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DR. GOLDMAN: Yeah.

DR. PICCIRILLO: One of the other things that we wondered about, coming back to the timing and the amount of time that, that the subcommittee members actually have in their review, I think it may be true that, that some of these documents do arrive in exceptional time for the members to review them. But it's a matter then of the time available because if, I noted that there were a number of questions being raised by some of the committee members that were things that probably should've been considered, looked at earlier.

DR. GOLDMAN: Mm-hmm. (Indicating affirmatively.)

DR. PICCIRILLO: For instance there was a, a discussion about whether genotoxicity data are relevant to the carcinogenic process. And it was obvious that no one really had taken a look at the weight of evidence approach to using gene tox data that EPA had promulgated a number of years ago. So, the, the lack of genotoxicity for Naphthalene just seemed to be discarded. So

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it's just some of these sorts of things made me at least have a sense that, that many of the committee members, the committee members are working in the thick, but in some cases they may not have really had the time...

DR. GOLDMAN: Yeah.

DR. PICCIRILLO: ... to completely get involved in the issues.

DR. GOLDMAN: Well, let me provide you with a bit of reassurance having worked with science committees like this a lot over the years and scientists of fairly high caliber and I've never seen a s...you know, a group like that who, you know, somebody at the last minute throws something over the transom, and it doesn't contain data and... that's what you described, that that would sway them away from looking at data that they had reviewed and, and I, I, you know , it must have been painful to watch that, but I don't believe that that kind of stunt, whatever it was that you observed, would have distracted a group of scientists from the actual data that they were looking at, and I think that's

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important, you know, for you to hear. And, and also that, by the way, there, there has been a change since EPA promulgated those guidelines some years back in terms of, you know, an earlier belief that all, all carcinogens are genotoxic agents and, and a greater degree of sophistication that genes, gene expression can be affected in many ways, in ways that cause cancer without classically being quote, unquote, genotoxic in terms of the in vitro tests and so forth, which I'm sure you're aware of. Why don't I go ahead and open it up for comment? I don't know if anybody...um, yes?

DR. MOURE-ERASO: Well, first of all I would like to caution Dr. Goldman to accept one description of what happened as what happened.

DR. GOLDMAN: But I wasn't there.

DR. MOURE-ERASO: Exactly, I, I was a member of the committee and I disagree with the perspective that is being presented here. I don't think that in any way, the, the, the evidence that was

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available for everybody to discuss. The.. It happens that, that, that the person that was a member of the panel, was the chair, has done studies in his group of study in UCLA and presented this data as one scientist making a comment on, on Naphthalene and this was presented as any other evidence that everybody else presented. And, and I really reject the characterizations of lack of transparency or attempt to influence the votes of people, I think it's insulting to say that. And the transcripts of the meeting are available and I recommend that everybody that is interested in this should read it and you'll see exactly what happened there.

DR. GOLDMAN: And I, I didn't mean to imply that I was accepting any one version of it, but I certainly can see that from the perspective of our presenter that what happened there didn't feel that way and, you know, so this is one of those disputes that we're not here to settle. We're really here to see if the process has a problem in.....

DR. PICCIRILLO: Yeah, I, I

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think where, where our comment comes in is the fact that we have a very short time in which to make our presentation. Had this document been submitted as part of the public comments, it would have been available to us. It would've placed us in a position where our 7 minutes would've been spent discussing that document and the relevance of that document rather than spending the 7 minutes discussing some issues and things which were already covered within the background document itself.

DR. TORAASON: This may not be a fair question, but, you, you mentioned advocates and it was mentioned earlier in the, in the day, but there was also the, the idea of expert panels. Don't expert panels by their nature have advocates on them and how do you resolve that?

DR. PICCIRILLO: That, that very well may be true, that depends on the make up of the, of the panels, depends on, on the selection process for putting the panels together. So...I don't know if there is a fair way of putting together a non-

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seemed that there was a, a situation which maybe could've been controlled better.
DR. CARPENTER: You and the speaker before talked about limited time of discussion, it's been my experience that that's really not the case. Do we ever have a time limit on a particular chemical? Didn't we discuss talc for the better part of a day without being cut off and saying, time is up? As long as new information was being offered and presented, the Bo..., the Board was listening to it and I, and I don't know where this idea of a set time came from.
DR. PICCIRILLO: Well, actually Dr. Portier mentioned that this morning that one of the changes was going from a 5 minute time period to a 7 minute time period.
DR. CARPENTER: Comments from the public, but I'm talking about the review process. Then you, you said the Naphthalene committee was given an hour and a half to consider all of this information and I never, I don't remember having been on ...

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DR. PICCIRILLO: Well, no, actually, I think what Dr. Le Huray said was we had a, we ended up because of the timing with the RG2 coming up, et cetera, we had a period of about 10 days to do our, our public comments. So...
DR. CARPENTER: But you yourself during your presentation made a comment about not having adequate time to present to the Board because of, of constraints. I mean that doesn't, that doesn't make much sense to me.
DR. PICCIRILLO: But no, that's...to the, yeah, this is to the subcommittee itself. We had , we had a 7 minute time period in which to present comments. We had submitted all of our, our written comments prior to that and when you've got that 7 minutes, it's very difficult to determine which issues you want to discuss. So the earlier comment that I made was if we had seen other public comments, and there were some concerns that were raised, that would have influenced how we spent our seven minutes before the

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subcommittee.
DR. GOLDMAN: Yes?
DR. PORTIER: I, I want to make sure I clarify one issue. The chairman for any given meeting of the NTP Board of Scientific Counselors is just the chairman for that meeting. There is no permanent chairman for any of the meetings. We always discuss the issue of who should be the appropriate chairman and again, to make the record straight here, for the Naphthalene situation and to give you a little more insight about how we run the Board of Scientific Counselors RoC meeting, generally the chair does not vote at the Board of Scientific Counselors Report on Carcinogens Meeting because they feel that if they were going to vote on such an issue they become an advocate and they can't properly control the discussion between, in the Board to bring out the, the issues that are being on. They, they're concerned that they might be somewhat biased. If any chairman for any particular meeting does in fact express a strong desire to enter into the debate on an

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issue and to vote on that issue, we discuss very carefully with that chairman whether or not they should chair such a session because we are very concerned that they might control that session. So in this case, for this particular session, this person was not chair of the, of the particular meeting from the start to finish. They stepped down for the entire Naphthalene discussion. And you will see that happen again, if it ever occurs, simply because we, we feel the, there's greater concern on our part for them dominating the meeting as chairman than for just entering into discussion with the rest of the Board.
DR. GOLDMAN: Thank you for that clarification. That sounds much more appropriate. It's, it's good to hear that. Other comments or questions?
DR. MOURE-ERASO: One last comment. For the record, I find it curious that you say that the person that made a presentation did not have any expertise of Naphthalene when one of the most respected papers on Polycyclic Aromatic Hydrocarbons

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as been, he, this person has been an author, he's considered an authority on air pollution and Polycyclic Aromatic Hydrocarbons and the record is clear about this and to say that he didn't have any expertise with Naphthalene, I consider preposterous.

DR. PICCIRILLO: No, the comment we made was, we did a, I, search of his, his li..., of the literature published by this particular individual and none of the research was on Naphthalene per se.

DR. GOLDMAN: I think I'm going to call a time out for this, okay. They can take it outside or whatever, but...seriously, I mean, we're... we really, you know, we really appreciate your comments and, on the process and I think that it, I think that it's, it's quite helpful. Are there other questions or comments for this presenter? If not, I'm going to invite you to sit down and, and, I've taken a little bit of time here to summarize some of the things I've heard and I thought maybe I could kind of walk through that and then open it up to make sure that, you know, that

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we have, that we've heard what everybody has to say. Read what document? No, I'm not going to read that document. We're, that, we have virtually read that document into the record. So, so some very, very quickly, very quickly and I've kind of arranged these in order of the, of the process. Obviously very consistently during the day, I think we've heard a lot of support overall for the process of listing of carcinogens through the concept that carcinogenicity is an attribute that is in, intrinsic to a chemical, that there's a weight of evidence approach that should be applied and that the listing process has public health value. Broadly, of course that the public should be involved early and as often as possible, that they should be striving for full transparency and more time somehow for discussions back and forth, discussions throughout the process. Specifically with the nominations process starting at the beginning, there was a question raised as to whether there was some way to bring in public input into the nominations process other than the fact that

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the public actually makes the nominations but in that selection process. Secondly, it was raised that the scientific review process perhaps could be improved. Now we've heard that the NTP already has established a goal of a 45 day period where the background document is out there for review, to give an opportunity to read it prior to the, to, for everybody to read and maybe comment for the RG1. However, there are some other ideas that were put forward such as perhaps that even more subject matter experts might be involved, such as revising the background document at each stage instead of appending the changes that occur at each stage to the document, whether you rewrite it or append seems to be an issue. And even to as radical of a proposal of getting rid of the RG1 and RG2 processes in, in essence and replacing them with an expert panel that's more like the Panel for the CERHR which is changing, but might still be seen by some as being a preferable process to the RG1 and 2 processes. Some issues were raised about the role of the Board of Scientific Counselors.

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I think some of those ended up in getting a better understanding of how the BSC actually works. But some of them had to do with perhaps even more time for them to deliberate on individual chemicals, perhaps more time for people to give presentations to them and have back and forth dialogue with them. And of, to an extreme of perhaps cutting the BSC out of the process and having those interactions occur with the expert panel, in essence that the expert panel would encompass, you know, the RG1 and 2 and 3 processes all into one process, which then I suppose a la CERHR would result in something that the whole BSC would look at as opposed to having an RoC subcommittee. Some questions were raised about the next step which is the role of the Executive Committee for the National Toxicology Program, you know, what is that thing and what does it really do and I think from what I've heard, comments ranged from either, you know, better defining that role, to make it more, more understandable to, to actually eliminating the Executive Committee from the

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process. I will say, you know, my two bits in this having participated in various elements of this is that, if there weren't an Executive Committee to look at these listings at this stage probably whoever is directing the NIEHS would want to invent one, because of just the need to vet these decisions among all the part..., parties that are a part of the National Toxicology Program before taking them to the Secretary in the Department of Health and Human Services which is a big step, and there are a lot of agencies in the department who care about this, and those agencies need to participate somehow and it is a, it is a forum for that and I think that it would be a real loss to the process to cut that out and I think you'd end up with processes that would be less out in the open and less direct and probably less well informed by the science without having the Executive Committee, that's just my opinion. A lot of questions came up with the interface between this process and the Risk Management Process. And it was pointed out that, you know, that

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there's even a state government in our country, California, that has regulations that directly incorporate the decisions, the listings of the RoC into the regulatory processes and that case for proposition 65, that there is sometimes a public health duty to put the listing into perspective and I think that that's a place where I think we've heard today that the NTP has taken that into account and that that has happened now a couple of times with pharmaceutical agency, agents like Tamoxifen. But again, Dr. Goldstein recommended publication of an actual notice around the time of the, of the NTP RoC listing, that would give, give stronger signals about where the regulatory agencies are going with that. And this is a bit out of the purview of the NTP so far, and, and again my two bits worth is that's probably a good thing because one of the things that has probably made this process so successful over the years is that it is not a regulatory process, that it's a scientific process and it's not, not embedded in a regulatory agency. Another, a number of

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other comments were made throughout the day about the issues of peer review and the quality of, of the data, and again, just my perspective, but I think it would be hard to point to a process either in the government or outside of the government where there's been a higher level of peer review or a higher degree of attention to the quality of the information that goes into these reports. And I, you know, I think that one would need to proceed with great caution before changing this process because it, it really has been extraordinarily successful in being a very high quality, very highly respected process. And just to go back at, at the, in closing to Bernie Goldstein's quote of what I said in 1999 and I would still say, and that is that this is a process that really has focused on the science and bringing the science into a weight of the evidence approach to determining carcinogenicity. It's not a process that's done for the sake of process. And that, that it's probably important to, to maintain. Obviously there are some changes that are gonna need to be

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done but fundamentally the public health value of this process needs to be honored in the process of considering those changes. Are there comments on, are there points that I missed in that summary that need to be brought out, other issues that, that people heard that need to be brought forward? I'm kind of opening it up for a bit of discussion on that. I was going to call on...

MR. KELLY: Would you like me to come up or...?

DR. GOLDMAN: What?

MR. KELLY: Would you like me to come up, or...

DR. GOLDMAN: No. Speak from the mic is fine. Just...and identify yourself.

MR. KELLY: Well, I've been debating whether, there is an issue that has not come up and it's, it's an important issue I think, I've been debating whether to even raise it because it's a bit of a can of worms, has to do with the criteria for listing a known human carcinogen. And the

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clarification that's given for that, and what's important to know is that that clarification itself has been interpreted and that when you consider the interpretation, the clarification is not clear. Now what the, what the criteria for known human carcinogens says is you have to have sufficient evidence from studies in humans to establish a causal relationship. And then the clarification says you need, this means you need evidence from studies, actually it says studies of humans rather than in humans. It doesn't say sufficient evidence to establish a causal relationship, it just says you need evidence of studies of humans. But then it adds a second paragraph that says there is a summary paragraph that applies to both the known and the reasonably anticipated criteria that says consider all relevant data. Now that, when that first came out, that was in the Federal Register Notice in 1996, the all relevant data language. We did not consider it that important because relevant seemed to refer to whatever was stated in the criteria. If it's relevant for known, you

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consider if it's relevant for what's said reasonably anticipated cri..., listing criteria, you consider that. Then when we got to the dioxin listing, what happened was there was a background document that said the basis for the listing is a combination of three things, human epidemiological evidence, which the background document said was not sufficient. It was limited. Animal experimental evidence and in vitro mechanistic data indicating that there was a similarity between the mechanism for animals and humans. So there was not sufficient evidence from studies in humans but that insufficienc..., insufficiency was compensated for by animal and in vitro data. And that was justified on the basis of this final paragraph that says, we can consider any relevant data. So in effect what it said is you don't need sufficient evidence from studies in humans. If you've got other evidence that will compensate for insufficient evidence, that's evidence in the form of animal evidence or in vitro data that all adds up to mechanistic data. So

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when you consider what happened there and the interpretation that's been put on it, and I'm sure this will come up again some time in the future, that clarification can be considered quite ambiguous. And I wanted to point that out and it may be necessary to make a clarification of the clarification.

DR. GOLDMAN: Well, I'm not saying that I agree with you that it actually says that, but I'm remembering now that also Dr. Sass raised the question about further defining the situations under which human data other than epidemiologic data would move a chemical up into the known category and, and so I, I think that that's another thing to add to the, the summary. It's another issue and, and you're raising it from a different direction. And, and the need to have it be, if you may, equitable in terms of those, you know, the kin..., the data can cause you to down grade a chemical, you know, and what can cause you to upgrade it and I think if Dr. Sass were here, that's the point that she would raise again, so I, but, we, we should add that, that issue to

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the list because it seems that that is still a live issue. Other, I know there were some other hands... yes?

MS. FELTER: Susan Felter. I have a couple of questions that evolve around the issue of exposure and the first one is, is really a question in terms of whether a draft document is considered to be adequate or not to move forward? The sense I got from the discussion was focused more on the, the toxicity side of it. But if I understand the mandate correctly, the list of substances that must be published is based on those that are known or reasonably anticipated and to which a significant number of persons residing in the U.S. are exposed. Is that better defined somewhere in terms and, and has that ever been a basis for deciding that something is, documentation is not sufficient to move something forward because there's inadequate information on the exposure side or where do you find a better description?

DR. GOLDMAN: So your question is are there chemicals that have

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been nominated that have not been moved forward because of a judgment that there are not a sufficient number of people in the United States who are exposed to that chemical? Does anybody from the program know? Bill, can you, can you answer that question?

DR. JAMESON: Yes, as a matter of fact there have been a couple of chemicals that were listed in the first Report on Carcinogens that were subsequently removed from or de-listed from, from the Report on Carcinogens because it was determined that there was no longer any human exposure to that material. So it didn't, since there was no documented exposure to those materials, they were removed even though there was strong, strong evidence that, that it was an animal carcinogen.

DR. GOLDMAN: Which materials and which chemicals?

DR. JAMESON: I'd, I'd have to look at the report, I can't really...

DR. MOURE ERASO: I, I don't remember a, the specific chemical but one

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thing that, that concern me about that as being one criteria is that there might be the, the mistaken conclusion that that particular chemical might not be a carcinogen or it doesn't have cancer effects when in reality the only criteria that was used, not to have studied, is that there is no exposures in the United States. Meaning that if there are not exposures in the United States, it doesn't matter if it's carcinogenic or not, which, I found it a little strange to say that and also probably the language could be changed in a way that, that to make it clear that nothing is being said about the carcinogenic effect of the chemical one way or another, simply it has not been studied. Because there might be the possibilities of having that confusion.

SPEAKER: Actually that language can't be changed because that's the law. I mean, that's the one we've always had to deal with that issue, so...

DR. MOURE-ERASO: The language stays basically.

DR. GOLDMAN: Go ahead.

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MS. FELTER: Yeah. I'd like to continue with my question about exposure, it goes back to I think the very first opening statement that I've heard a couple of times that cancer is intrinsic to a chemical and I find that to be a very interesting statement to not have controversies surrounding it because as we all know there is species specificity, metabolic differences such that one strain, one specie may be, it may be intrinsic to a male rat but no one else, may be associated with high doses and not low doses, example of lung cancer associated with particle overload. So a chemical that demonstrates some tumorigenicity or carcinogenicity under specific situations, to say that now it's an intrinsic property of the chemical...if you could address that a bit?

DR. GOLDMAN: Well, I should've said the ability of the, of the chemical to cause cancer in a human and I think that that issue that you raised about species differences has been addressed and for quite some time actually in the way that

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data that are relevant to species that might support the notion that the risks for humans are different than risks for other species, and has been incorporated and can be used, has been used to downgrade the classification of chemicals just as those same mechanistic data in humans has sometimes been used to upgrade the classification of a chemical. So, that's, that's a part of this process.

MS. FELTER: May I? I, I certainly agree, and I've seen many examples of where that is true, certainly with the species differences. What might be less obvious to me and, and maybe the question of genotoxicity to some extent comes in here is the relevance of findings at higher doses and not lower doses, where from the amount of information that's available on the Report on Carcinogens, again, with the goal being public health, if there's no distinction made between, you know, there's no dose information included in here to indicate that this chemical caused tumors in these bioassays or these studies under these conditions. It's simply a statement that it

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caused tumors, boom. Which when you really get into it from a toxicological perspective, the implications of finding tumors under one set of circumstances versus a different set of circumstances in terms of the public health implications are quite different. And so has there been discussion about, and maybe this goes beyond the scope of this, this meeting.

DR. GOLDMAN: No, it, it really isn't. I mean, it's, it's, I think that it's been an ongoing issue for probably from the beginning of the program and the way I would encapsulate the issue is, is it okay that the Report on Carcinogens stops at the hazard identification stage or should they take a next step and do dose response modeling, you know, come up with potencies or, or come up with judgments about what would be the appropriate dose response curve and whether there might be a threshold and so forth and so on. And at, at this point in time there may be comments and I think that the NTP folks can talk about that, sometimes there are kind of comments about

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some of that, but once NTP makes the judgment about classification, it's up to the individual agencies to go through processes of attempting to determine exposures, dose response modeling and so forth and they don't always do those things the same way to even, even further complicate our lives. So this has, this has been an ongoing issue and, and it's been felt that by stopping short of that, that it, it clearly draws the line between this process and a risk management process, but I think it's always going to be an issue. Chris?

DR. PORTIER: I just want to make sure I, I'm understanding the comment, now this is a comment on the RoC document itself because obviously the background documents spent a considerable amount of time talking about the context of the observations which are being reviewed and so the question is to what degree does all of that information then also get characterized into the rather short listing that goes into the Report on Carcinogens. And certainly every re..., every report we visit the discussion

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about how do we present this material and to what degree we might try other things, so I think your comments are useful and we, we will follow up on them. One of the reasons we are now very vehement, I personally am very vehement about the background documents becoming sort of something that is permanently there for people to look at and review and see the comments and see the process that went through is, it's actually that that puts the, the report of, Report on Carcinogens listing into context. It's really hard in a short document that isn't the entire book of the background document to break it all down into something clear and so the background document then plays a more important role as do the comments on the background documents and the minutes from the meeting and the discussions of the votes, et cetera. They all become something that place the listing in context. And so we're working on it, it's just not an easy issue.

DR. BABBAGE: Yeah, Michael Babbage from CPSC and I just wanted to comment mostly on Dr. Goldstein's very

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interesting proposal but also a little bit on this last comment is, as it stands now when a chemical is listed in the RoC, it doesn't automatically trigger any regulatory action in at least at CPSC, and when we do evaluate potential hazards we of course consider the RoC, IARC and the CERHR and, and, and so on, but the, but our policy has always been that we do our own evaluations of everything from hazard ID to the, to the risk and risk management, so really the, the bottom line is that the bur..., the burden is on us, on, on the regulatory agencies, or in our case on us in particular to, to do the, the, the, the next three steps of the risk assessment essentially and to, and to say whether a particular product in our jurisdiction is a hazard and I mean, that's, that's how it is and whether that should change, I don't know, but that's the way, that's how it is now.

MR. KELLY: Of course, this, this issue came up the last time we had a public meeting on this in, in 1999; that is, the issue of to what extent should the

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listing information on the Report on Carcinogens give some information about dose or exposure and what is known about carcinogenicity at a particular dose or exposure, to what extent does that knowledge depend on there being a certain level of dose or exposure. Since that meeting we, we do have new legislation and guidelines in the form of the Data Quality Act and guidelines and one of the requirements of that is utility. Utility is defined as utility to the intended, for the intended purpose of the information product. We've discussed this before when you go back to the legislative history of the Report on Carcinogens, it's very clear that Congress intended that this report have utility for individual Americans who would make choices about their personal lifestyles and exposures. And yet at the very, in the introduction of the Report on the Carc..., on Carcinogens currently it says that there's nothing in the Report on Carcinogens is intended to necessarily have any relevance to the activities of people in their daily

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lives and there have been occasions when the, there have been critical issues regarding dose and exposure that have come up with regard to specific listings and the review panels, particularly the RoC subcommittee have been instructed by RoC staff that they should not consider dose or exposure in making recommendations on the listings. The one that comes most prominently to mind as a good example of this is, which I no longer have any interest in other than my daily personal life as an individual consumer is the consumption of alcoholic beverages, in which there is considerable evidence that very moderate intake of alcoholic beverages is not carcinogenic and is actually has health benefits, mainly in the form of having to do with heart attack and stroke. But the point is that, and this was raised and debated considerably among the RoC subcommittee members is that the evidence we have that shows carcinogenicity with alcoholic beverages; that is, what we were already shown as known to be a carcinogen only has to do with people who are what they

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called, pursue an alcoholic lifestyle. That is, they're very heavy drinkers and have all the other things associated with an alcoholic lifestyle of just general dissipation, poor diet, lack of exercise, you know, lack of productive work, that sort of thing, possibly low socioeconomic status which has been correlated with increased risk of cancer, et cetera. And yet the, so the implication of this would be that the listing should say that alcoholic beverages are known to cause cancer among people who are heavy drinkers or who are, who are, pursue an alcoholic lifestyle, something like that. That was the debate and yet they were instructed that they could not insert that sort of language in the Report on Carcinogens and they should not even consider it as part of the information product because the Report on Carcinogens is only a hazard document, doesn't consider risk. I think this issue now with the new legislation...

DR. GOLDMAN: Bill, I don't believe that's what the committee concluded about the literature on alcohol, but, you

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know, I might be wrong, it's been a few years, but I don't think that that really was their conclusion.

MR. KELLY: Oh, I don't know about the conclusion, I'm talking about the...

DR. GOLDMAN: That, that the risk for cancer was only among these subgroups that suffer from all these other conditions. I don't think that that was their conclusion. So I, you just have to be careful here but...

MR. KELLY: I didn't say they concluded that, I said...

DR. GOLDMAN: Yeah.

MR. KELLY: ...they were debating that and then they were told that that was not even appropriate to get into and it was not necessary to debate. So they never really reached a conclusion on it. But it was an imp...it is an important point. It, it comes up with, very prominently with some other listings that are in the Report on Carcinogens now. And I think it's going to come up sometime with the new legislation

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and guidelines and should probably be dealt with at some point. And the usual response is that they're, you know, we don't want to get into quantitative risk assessment and dose response curves and the usual, you know, things that regulatory agencies get into and I don't think you need to do that. I think a, there are broad qualitative sort of dose response or exposure statements that can be made about some of these chemicals. You know, for example, on some of them you could say that, you know, cancer has only been found, is, is only known to have occurred in worker populations that were exposed to extremely high doses as a result of industrial accidents. You know, if that were the, the case rather than in the general population, rather than saying it's giving the implication that it's known to cause cancer among anybody who's exposed to this. But again, I would like to point out that we, we do have some new law on this particular issue. There is very pertinent legislative history. It's never really been confronted adequately I believe by the

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agency. I found the response to the public meeting comments in 1999 to be very dismissive in fact of this particular issue. And since it has come up, I do feel that this needs to be pointed out at this point. Thank you.

DR. GOLDMAN: Okay, well, I guess that's another issue to put up there, but I, I should say that I have not yet heard anything either here or elsewhere to say that there's a determination that the Data Quality Act applies to this process so, I , but I think that your point about trying to put the, put it in somehow in context with exposure and I think it get backs to the point that was made earlier needs to be, you know, added as one of the, one of the issues that was raised. Are there other issues that need to be identified as coming out from, from this meeting? Make sure that we're not leaving anything out.

DR. MOURE-ERASO: I mean, I, I, I read what you presented as the summary of the issues and I, a little unclear about it, the way that you presented this in order

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of priorities or is it a list or, or, or how?

DR. GOLDMAN: I tried to put it in the order of the process. So starting from the nomination through the scientific review through bringing it forward to the Board of, so I tried to just put it in the, in, in process order.

DR. MOURE-ERASO: Yeah, because of, of, I probably will have, as, as probably the people here in the panel have different levels of, of reactions to these statements that were presented, I mean, it doesn't seem that, if the panel is going to react to the issues that were presented, there will be different opinions I assume.

DR. GOLDMAN: Perhaps it would make sense at this stage to, you know, turn to the members of the panel to see if you have some feedback that you know, your own reactions or, you know, further points that you want to make to be sure to put them in here now. There will also be a written report and an opportunity in that to, you know, after we've had a chance to ruminate

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further, to, to add to that. So, do you want to lead off on that?

DR. MOURE-ERASO: Sure. First of all I, I, I hear with some trepidation the proposal of a re-configurating the procedure, the process of, of conducting the business of the NTP. Specifically the, the recommendations of basically eliminating the R, RG1 and RG2 and the Board of Scientific Counselors. I believe very strongly that the appropriate function of the science in the federal prog..., in the federal government that exists in, in NTP is to take the responsibility of the process of making decisions that eventually are going to have big public health impacts. And I absolutely reject the notion that we can privatize this process. The expert panels as it was described here constituted mostly from the industry that supposedly is being affected by these decisions is in my mind absolutely not an improvement in the process, but the opposite. I also believe that one of the things that is also of great importance in terms of having a fairness in the way

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that mechanistic data are used as you mentioned, what Dr. Sass mentioned that there is a need to have explicit descriptions of how mechanistic data can affect a process, upwards and downwards and that that should be made specific in the language, and not only put an example of how things could be de-listed and know how things could be changed from one classification to another. And specifically to, to maximize the appropriate use of mechanistic data, to properly inform people of, especially properly inform exposed people what to expect in effects of carcinogenicity.

DR. DELZELL: I'm sure that each of us on the panel has a slightly different view of what's transpired and what our reactions are. I, I do, I have heard some very specific recommendations for clarifying and improving the process, and I think those need to be carefully considered. I am not as willing to, not dismiss but, but have a negative reaction to the idea that the whole process be reviewed and perhaps changed. I think that it is very good to

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consider changes, particularly in light of the very sweeping changes that we see taking place in science or are about to take place. I, I do feel that the peer review process can be improved. I'm less sure of the specific mechanism for improving the peer review process. The, the other thing that we've heard quite a bit about today is the, the need to improve the exchange with the, between the public and the peer review process. And I'm sure that that can be improved also.

DR. CARPENTER: Yeah, I agree that, I think that there is a fundamental misunderstanding about what the peer review process is because we encounter the same arguments. A number of the discussions that have taken place today take place in the RoC meetings themselves. Particularly questions about exposure and the idea of listing a chemical, realistically exposures will never occur to humans, so they're, they're, or they're at least not likely to occur. So that the actual risk that's being posed by these chemicals in everyday life is, is

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minimal. And I think that the Board gets an understanding of that issue, I think that the industry that's being affected and impacted by those decisions understand that issue, but I don't think that in general very many other people really do, that a lot of times with, when you're, when you're dealing with state agencies in particular, if you see a chemical listed as a carcinogen, it's an immediate problem, and that's, that's clearly not true. And I think there, there, there should be a mechanism whereby some of those reservations can be expressed and I've done this in, in RoC meetings as have a num..., number of other people. It's in my understanding not part of the mechanism now, but I would really like to see it part of the mechanism whereby a description says, you know, it's, the apparent risks from this exposure to this chemical are small, but this is a hazard identification process and I think that get, gets lost a lot of the time in discussions is that, is that this is limited to hazard identification and I think that's a real issue that's going to keep

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coming up until it gets addressed formally.

DR. GOLDMAN: Mark?

DR. TORAASON: I think, there was a lot of discussion about the document, I'm not sure that, that the review documents met the same, serve the same purpose as the reproductive health effects documents. I mean, the documents that the NTP uses are to facilitate the review by the Board of Scientific Counselors and the different regroup, review groups, and over the years those documents have been improved and it's sort of coming back to bite the NTP because the better they get, the more people want them to be better, the more they want the process to be better. And if that's an int.., if that's the intent, to produce an, a comprehensive document, then some of the recommendations we heard were great. But perhaps maybe the focus should be on the writing that appears in the Report on Carcinogens because that's the thing that really goes forward, that's the thing that most people read. And that isn't given a review process that I'm aware of, it just

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sort of appears. So maybe that, that could be a place of focus. The other comment I, I have, that I think there, there are some really good recommendations about the time allowed, I heard some things from a perspective that I hadn't noticed before and one particular point is, I've attended a lot of meetings and it's invariably there was plenty of time for everybody to say what they want. There were a couple of meetings where people were cut short and I was thinking, what's this concern about time? But I, it did dawn on me, when you're told ahead of time you only have 7 minutes, you only prepare 7 minutes. I guess if you're savvy about what goes on in the meetings, you can prepare for 30 minutes and 40 minutes, so... And the other point was what Hillary made about, oh, we get these documents two months ahead of time, that's true, but I'm more sympathetic toward the people that want to respond to that. They have two months, they have to write it and then we get it in at the last moment, and then they feel that because reviewers got it at the last moment

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they didn't get much of a chance. And I think so, even though I may get the document two months ahead of time which gives me plenty of time, not plenty of time, but adequate time to review, I'm realizing that there's also this other gap where people want to not only review it, they want to comment on it and they want me to have time to review what they say and maybe there is need, a need for a little more time there.

DR. GOLDMAN: Excellent. And I think those last points are really points that should have been in my summary too, that, the re..., the idea of the review of the actual listing was a very interesting idea, I don't know exactly how you would do that, but there might be some way at least, you know, minus the judgment call, the description of the substance and the description of the toxicology, maybe that could be vetted fairly early, that's kind of an interesting idea. What I want to do now is turn to first Bill Jameson, he has some additional information for the record to give us and then ask Chris Portier to sum up.

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DR. JAMESON: Yeah, just, just for the record, I'd like to identify the fact that we received additional written comments for this process meeting from individuals who could not attend. We've received these, these, the written comments and they were placed on the web as part of the public record for this meeting, but, but for, for the purpose of the record I'd like to identify that Sam Cohen of the University of Nebraska Medical Center, Neil King of Wilmer, Cutler, Pickering on behalf of the Nickel Production Environmental Research Association and Inco United States submitted comments, I'm sorry, Samuel Cohen submitted comments, Mr. King submitted comments, Wulf Utian of the North American Menopause Society submitted comments, Dr. Lawrence Robinson from the Color Pigments Manufacturing Association and James Enstrom from the University of California at Los Angeles submitted written comments. These were made available on the web, distributed to the panel and, and copies are also available outside.

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DR. GOLDMAN: Thank you.

DR. MOURE-ERASO: Dr. Jameson, there were some other things, there were some other things that were distributed here that were in part of the written record too...that will appear in the, in the final list?

DR. JAMESON: Yes, yes, every, everything that was distributed from, from individuals who were, were scheduled to make presentations but were unable to and submitted their, their, their comments, those will also be made part of the record, yes.

DR. PORTIER: I thank you all, Lynn, thank you very much for running a very interesting meeting and I, I actually look forward to the written part of this, bulleted it's good enough, I, I think we've got a lot of the points down that you brought forth. I'm going to clar..., I was, I've been debating whether to clarify an issue or not, but I, I can't let it go. Sometimes at public meetings things are said that get carried away and everyone leaves with the impression that's an incorrect

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impression. So I'm going to pick on alcohol. Because I really want to make it clear that we do go to some degree of effort to try to clarify our listings. I'm just going to read one part from the alcohol listings, so, so you can all go back and do your homework and read and look at this. The second sentence on the alcohol listing, the first sentence clearly says, alcohol is a known human carcinogen, according to our review of the second sentence it says, studies indicate that the risk of cancer is most pronounced among smokers and at the highest levels of consumption. I just want to clear, make it clear that the, we do take into account the issues that have been debated, the last part of this, we do draw a line about where we're going with dose response. In some of our presentation there are issues that clearly become very difficult issues that being an expert in dose response and having spent 25 years of my life doing research on it, I recognize some of the difficulties involved in making decisions about what level constitutes concern and what level does not

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constitute concern. We're always willing to consider where we're going with that but I really don't see us ever, unless legally required by Congress directly, going into the issue of setting thresholds and standards and things like that. It's just not the mandate of the Report on Carcinogens and I believe, my interpretation and my counsel will correct me at some point is that that would take us way beyond the mandate of the law for the Report on Carcinogens and I just don't see us going there. But the comments have been very stimulating, there's a lot of things I will take back to staff and look at very carefully. We, we always look at how we list the criteria and we are constantly trying to redo that. We always very carefully look at how much time we've given you in, in providing additional comment to us up front because we really do believe it's the debate, both the debate that occurs at the public meetings, the debate that occurs at the government meetings and the debate that occurs in the written documents that drive where the, the program is going to go in

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recommendation for a listing or non-listing in the Report on Carcinogens. It's very important we get that record very clear and there's been some excellent suggestions here on how to improve that record and improve that debate. And I think we'll be looking very carefully at how we do that. Again, thank you all very much. I want to thank Dr. Jameson and his staff not only for this meeting but for years and years and years of effort in putting together the Report on Carcinogens, creating over the course of, 20 years of your career now, Bill? Over 20 years of process that I think is second to none, not only in the U.S. government but in the world. I think we've got a process that is more open than any other decision process for hazard I've ever seen and I've been involved in a lot and we continue to try to make the, make it better and I think it's Bill and his staff that have taken us there and I want to thank them very much. Thank you all for being here. Thank you very much for your comments. Again, if you have any additional comments or anything else you'd

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like us to consider, we are always open to comments even after the close of this meeting. Contact Dr. Jameson, Dr. Wolfe and get them to us. And again, Lynn, thank you very much and I'll turn it back over to you now.

DR. GOLDMAN: Well, and I think all of our thanks to Bill Jameson and the NTP staff for the work that they do on the Report. Obviously, it's something we all appreciate and that's why people are here to try to help make it better.

DR. JAMESON: If I may, I'd like to recognize Anna Sabella of my staff who worked very hard for all the logistics of this meeting, and, and has done an excellent job in getting everything and I...

DR. GOLDMAN: Thank you.

DR. JAMESON: ... I'd like to thank, publicly thank Anna Lee. Thank you.

DR. GOLDMAN: Okay, adjourned.

(WHEREUPON, the Meeting was concluded at 3:16 p.m.)

CAPTION

The Meeting in the matter, on the date, and at the time and place set out on the title page hereof.

It was requested that the Meeting be taken by the reporter and that the same be reduced to typewritten form.